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## THE EFFECTIVENESS OF TYPHOID VACCINE PREPARED BY THE U. S. ARMY


COLONEL GEORGE R. CALLENDER
MEDICAL CORPS, UNITED STATES ARMY
AND
MAJOR GEORGE F. LUIPPOLD
SANITARY CORPS, ARMY OF THE UNITED STATES


Siler and his co-workers included in their monograph "Immunization to Typhoid Fever" [1] a historical review of the introduction and use of typhoid vaccine in the United States Army. Briefly, typhoid vaccine was introduced on a voluntary basis by F. F. Russell in March 1909. In 1911 antityphoid vaccination was made compulsory for all military personnel.

From 1909 to 1916 a monovalent typhoid vaccine was used, and from 1917 to 1927 inclusive the vaccine was of a triple typhoid (TAB) type containing typhoid, paratyphoid A and paratyphoid B components. In 1928 the paratyphoid B fraction was omitted, followed in 1934 by the omission of paratyphoid A. Monovalent typhoid vaccine was then used exclusively for antityphoid immunization until September 1940, at which time the paratyphoid A and B components were again added. This is the product now used for the immunization of all personnel in the Army; it contains 1,000 million typhoid bacilli and 250 million each of the paratyphoid A and B organisms per cubic centimeter.

The first typhoid culture to be used for the preparation of typhoid vaccine by the biologic laboratories of the Army Medical School was the "Rawlings" strain. This culture was isolated by British investigators from a fatal case of typhoid in 1900 and was being used by the British as a vaccine organism when Russell went abroad in 1908 to observe their methods of preparing typhoid vaccine. The "Rawlings" strain was subsequently used as the typhoid vaccine organism in the Vaccine Department of the Army Medical School from 1909 until late in 1936. During this time it had been maintained in an intermediate stage, neither rough nor typically smooth but tending toward smoothness in its cultural and antigenic characteristics.

### EXPERIMENTAL STUDIES

Late in 1934 an exhaustive investigation was begun to determine the relative merits, as immunizing agents, of several selected strains of the typhoid organism.[2] Out of this investigation there emerged a strain of Eberthella typhosa of superior immunogenic potency. This culture had been recovered from a chronic typhoid carrier in Panama, and since the first announcement of its use it has been variously referred to as "Boxill," "Panama carrier," "Panama 58" and simply "58." For the purpose of future reference it bears the official designation of "E. typhosa strain 42-A-58" of the Army Medical School culture collection.

This strain of E. typhosa has been used by the Division of Biologic Products of the Army Medical School since late in 1936 for the preparation of typhoid vaccine, and it is being used currently as the typhoid component of TAB vaccine. Briefly described, it is culturally and biochemically a typical typhoid organism, colonially and serologically smooth, highly virulent for mice, and antigenically complete with a high content of Vi antigen. Before its acceptance by the Division of Biologic Products it had been subjected to every test known to us designed for determining its qualification as a vaccine organism—mouse virulence, agglutinogenic activity and immunogenic potency—and, from the standpoint of production, rate of growth, emulsifying property and stability in salt solution. Added to this were comparisons of its toxicity in human beings with that of other typhoid cultures.

Tests for its immunogenic potency were conducted with test organisms recovered from patients and carriers living in various sections of the United States. When satisfactory evidence had been secured concerning its immunogenic coverage over domestic strains of E. typhosa, cultures from other parts of the world were sought as test organisms. Two of these foreign strains were obtained, one from China (province unknown), the other from Budapest. In both active and passive immunization tests a vaccine prepared with E. typhosa strain 42-A-58 produced the same high degree of protection against these imported cultures as it did against the domestic variety of the typhoid organism.

Recently the question of immunogenic coverage afforded by our typhoid vaccine organism has been revived in reference to strains of E. typhosa prevalent in the Middle East. A doubt has been expressed that our vaccine affords adequate protection against the local Middle East strains, and it has been recommended that the vaccine manufactured locally be used for the immunization of the United States armed forces stationed in that area.[3]

Although this hypothesis is advanced from time to time, it has few advocates among immunologists today. However, as a matter of interest the vaccine recommended, the typhoid organisms used and some cultures from cases of disease from the area were obtained for comparative immunogenic studies. These cultures were examined for mouse virulence, antigenic content and

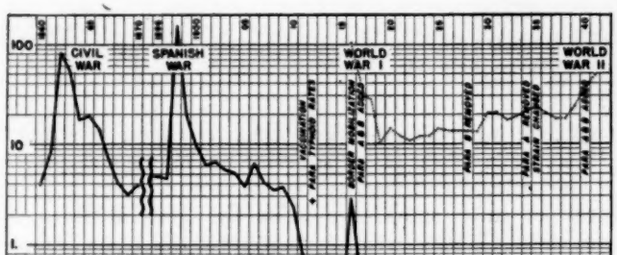
1. Siler, J. F.; Dunham, G. C.; Longfellow, Don, and Luippold, G. F.: Immunization to Typhoid Fever, Monograph Series, No. 17, Baltimore, Johns Hopkins Press, 1941.

2. Siler, J. F.: Typhoid Vaccine Studies: Investigation of Virulence and Antigenic Properties of Selected Strain of Typhoid Organisms, Am. J. Pub. Health **26**: 219 (March) 1936. Siler, J. F., and others: Protective Antibodies in Blood Serum of Individuals After Immunization with Typhoid Vaccine, ibid. **27**: 142 (Feb.) 1937.

3. Official correspondence.

immunogenic potency. In all determinations our vaccine strain 42-A-58 was included as the control organism in order to detect superiority of the imported cultures over our vaccine culture, should any differences among them exist.

All cultures (those from the Middle East and strain 42-A-58) proved to be of equal virulence; they were




Rates per thousand annually for typhoid fevers in the United States Army, 1860-1942. Dotted line shows rates for all diarrheal diseases, 1916-1941.

antigenically identical, and they were equal in immunogenic potency when either a domestic or an imported strain of E. typhosa was used as the test organism. It was concluded, on the basis of these experimental results, that our currently used vaccine organism is quite as effective an immunogenic agent against the E. typhosa prevalent in the Middle East as is the vaccine organism used there, and as are locally distributed strains of typhoid organisms in the Middle East.

As for the paratyphoid A and B organisms used in our 1940 type of triple typhoid vaccine, these were selected on the same bases as was the culture of E. typhosa. The strain of Salmonella paratyphi (41-N-22) was obtained from Dr. A. Felix of London and is easily the most virulent para A organism that we have found. It is culturally and biochemically typical of S. paratyphi, antigenically complete and immunogenically superior to all other strains with which we have worked. The strain of Salmonella schottmuelleri (41-H-6) was first chosen from our culture collection because of its high virulence for mice; and when it was shown to be an antigenically complete, immunogenically active, culturally and biochemically typical para B organism, it was adopted to represent the B fraction of our TAB vaccine. A fuller description of these strains has recently been published by the staff of the Typhoid Research Unit.[4]

## STATISTICAL STUDIES

The proof thus far presented of immunogenic coverage afforded by our vaccine organism consists of experimental evidence only. Much more significant is the statistical evidence. The actual morbidity of typhoid and paratyphoid fevers among the armed forces of the United States is shown in the chart covering the period from 1860 to 1870 and from 1896 to 1942.[5] The rate for 1942 is an estimate, since the actual strength of troops was not available. Rates for paratyphoid were first included in the Surgeon General's Annual Report of 1912, and some paratyphoid fever occurred in most of the years following that period. In 1916, during the mobilization on the Mexican border, an epidemic of diarrheal disease, including both bacillary and amebic dysentery, occurred there together with an increase in typhoid and a more pronounced one in paratyphoid, most of which was due to Salmonella paratyphi. The actual number of cases for that year were typhoid 96 and paratyphoid 410, approximately 95 per cent of which was paratyphoid A.

In 1917, with an average strength for the year of 678,579, there were 297 cases of typhoid, 13 of para A and 7 of para B, a total of 317. In 1918, with an average strength of 2,518,000, there were 768 cases of typhoid, 73 of para A and 34 of para B, a total of 875. Conditions in 1918 in the battlefields of France were responsible for a considerable proportion of the cases in that year, which included a number of contact cases among those caring for the sick.

An interesting test of the efficiency of the vaccine before the addition of the A and B fractions occurred in Hawaii in 1917. A patient with typhoid in a labor camp on the watershed infected an emergency source of water used only in dry periods. This water supplied a section of the post of Schofield Barracks, the population of which was about 4,000 immunized persons, most of them soldiers, and about 800 nonimmunized, most of whom were laborers—Koreans and Japanese. Fifty-five cases occurred in the group of 4,000 and 56 in the 800 unvaccinated controls. Eleven of the 56 were considered to be contact cases. Four of the 55 patients in the immunized group died, whereas there were seven deaths among the 56 patients in the unvaccinated group. This would indicate a protection from morbidity of about 80 per cent. Another factor believed to be of importance in minimizing the incidence in the nonimmunized group is that these oriental

*Comparison of Typhoid and Diarrheal Diseases*

| | Average Strength* | Admissions | Average Rate | Deaths |
|---|---|---|---|---|
| 1861-1866 | | | | |
| Typhoid | 532,198 | 79,462 | 29.86 | 29,336 |
| Diarrheal diseases | 367,742 | 1,589,126 | 687.49 | 37,806 |
| 1898 | | | | |
| Typhoid | 147,795 | 20,926 | 141.59 | 2,192 |
| Diarrheal diseases | 140,395 | 56,192 | 400.24 | 202 |
| 1917-1919 | | | | |
| Typhoid and paratyphoid | 1,501,265 | 1,742 | 0.42 | 238 |
| Diarrheal diseases | 1,501,265 | 92,512 | 22.41 | 268 |
| 1940 | | Admission Rates Only | | |
| Typhoid and paratyphoid | | | 0.02 | |
| Diarrheal diseases | | | 37.57 | |
| 1941 | | | | |
| Typhoid and paratyphoid | | | 0.02 | |
| Diarrheal diseases | | | 49.89 | |

* Strengths on which reports were adequate.

peoples seldom drink water straight, preferring tea—though their eating utensils were cleansed in unboiled water.

As a result of reports from abroad before our entry into the first world war and of the epidemic on the border in 1916, S. paratyphi and S. schottmuelleri were added to the vaccine. From 1917 through 1919, when considerable numbers of our troops were exposed in areas of relatively high endemicity, the rates continued considerably above those of the period just prior to

4. Longfellow, Don, and Luippold, G. F.: Typhoid Vaccine Studies: VII. Typhoid-Paratyphoid Vaccine, Am. J. Pub. Health **33**: 561 (May) 1943.

5. Annual Reports of the Surgeon General of the Army, United States Treasury Department, Public Health Service, 1943.

the war—from 1912 to 1915 inclusive. It is interesting to note that during the period of 1917 to 1919 the rates for diarrheal disease were dropping and reached the lowest point in the history of the Army in 1919. In the United States, troops were quartered in cantonments during their preparation and no extensive maneuvers were held. They were also demobilized from these same cantonments. The use of field sanitary installations for the disposal of excreta was minimal.

Because of the feeling that the para B fraction of the vaccine caused an undue amount of reaction, and because of the very small number of cases of paratyphoid B which were occurring in the countries where troops were stationed, this fraction was removed in 1928; and this was followed in 1934 by the removal of the para A fraction. The sharp rise in the typhoid rate in 1931 was due to 22 cases occurring in one organization which used unpasteurized and infected milk while on a maneuver. The number of cases of paratyphoid as well as typhoid were insignificant between 1919 and the present time, with the exception of the 1931 group. The removal of para A and para B fractions does not appear to have influenced the rates for typhoid and paratyphoid fevers, although the general level of the incidence of diarrheal diseases increased appreciably in 1930 from about 12 to 20 per thousand and did not recede in subsequent years.

With the mobilization of the emergency period, typhoid rates show no significant change in 1940, during which there was a considerable amount of activity of troops in the field utilizing improvised installations for the disposal of human wastes. But during this period there was a very distinct advance in the rates for diarrheal diseases, including bacillary and amebic dysentery, diarrhea with cause not specified, gastritis and enteritis and colitis and enteritis. The combined rates were 17.74 for 1938, 24.79 for 1939, 37.09 for 1940, 49.89 for 1941.

Increase in the diarrheal diseases is usually accompanied by increase in typhoid. This is especially true in armies operating under field conditions. The diarrheal diseases usually occur in the greater numbers, though typhoid has the highest fatality rate. The accompanying table compares typhoid and paratyphoid with diarrheal diseases for four war periods.

The result of vaccination in World War I as compared with previous wars is evident, though the diarrheal rates were only about half those of the prewar period exclusive of 1916. Rates for 1940 and 1941 only are calculable, those for 1942 being estimated because records of the strength of the Army are not available. Typhoid and paratyphoid fever rates in these years are insignificant, and this in the presence of rising rates for the diarrheal diseases. This picture can be interpreted only as definite evidence of the efficiency of the present vaccine.

### SUMMARY AND CONCLUSIONS

Following the compulsory use of typhoid vaccine in the U. S. Army in 1911, morbidity rates for typhoid and paratyphoid fevers dropped from about 2.5 per thousand annually in 1910 to below 0.2 for 1913-1915 inclusive, the Army having few troop maneuvers during this period.

In 1916 an epidemic condition of typhoid and paratyphoid fevers and diarrheal disease in the Army operating in the field resulted in rates for typhoid and paratyphoid fevers approximating those of 1910, most of the increase being due to paratyphoid A. No paratyphoid organisms were included in the vaccine of that period.

The rates for typhoid and paratyphoid remained well above the peacetime level of 1913-1915 during the three years of World War I yet were significantly below the peacetime level of the prewar period—about 3 to 4 as compared to 0.3 to 0.4.

During the peace period of 1919 to 1939 rates were in the range of 0.01 to 0.08 with the exception of the food borne outbreak of 22 cases in 1931.

Thus far, rates for typhoid and paratyphoid fevers for the mobilization years 1940-1942 are insignificant, and this in the face of a rise in the rates for diarrheal diseases to higher levels than the period preceding World War I.

With this evidence it appears reasonable to conclude that the World War II (1940 type) triple typhoid vaccine is considerably superior in effectiveness to the TAB product employed during World War I.

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## VISCOSE TUBING FOR TRANSFUSIONS

### A REACTION REDUCING MATERIAL AND A SUBSTITUTE FOR RUBBER

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AND
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CHICAGO

With the introduction of sodium citrate as an anticoagulant by Lewisohn [1] and the development of the modern technic of blood transfusion, this procedure became routine and easily performed. However, under the most careful conditions a small incidence of untoward reactions, principally chills and fever, has remained a disturbing factor. Untoward reactions of this kind may be divided into two groups: intrinsic reactions, arising from the infused blood, and extrinsic reactions, arising from causes other than the blood.

This paper deals with extrinsic reactions. It has been amply demonstrated that the febrile reaction is largely due to the inadvertent injection of foreign material into the blood stream.[2] Many theories have been advanced in an attempt to explain the febrile reaction that is occasionally associated with the whole blood infusion and, for that matter, with intravenous infusions in general. Able investigators working along this line have shown that the reactions arise principally from three sources: pyrogenic substances in distilled water,[3] impure chemicals used for preparing solutions,[4] and improperly or inadequately cleansed equipment.[5]

Even with constant vigilance and unremitting care in the preparation of the material used in the drawing and the administration of citrated blood, the incidence of febrile reactions is still from 1 to 10 per cent or higher.

In an effort to reduce the number of reactions following the administration of citrated blood, we first

From the Transfusion Department, Michael Reese Hospital, and the Michael Reese Research Foundation.

1. Lewisohn, Richard: Blood Transfusion by the Citrate Method, Surg., Gynec. & Obst. **21**: 37, 1915.
2. Wiener, A. S.: Blood Groups and Blood Transfusion, ed. 2, Springfield, Ill., Charles C Thomas, 1939, p. 102.
3. Seibert, F. B.: Fever Producing Substances Found in Some Distilled Water, Am. J. Physiol. **67**: 90 (Dec.) 1923.
4. Walter, Carl W.: Preparation of Safe Intravenous Solutions, Surg., Gynec. & Obst. **63**: 643 (Nov.) 1936.
5. Lewisohn, Richard, and Rosenthal, Nathan: Prevention of Chills Following Transfusion of Citrated Blood, J. A. M. A. **100**: 466 (Feb. 18) 1933.

eliminated the character of solutions and the manner of cleansing glass and metal parts as factors in the febrile reaction. The solutions in use at the Michael Reese Hospital transfusion department are commercially prepared and proved pyrogen free on test, and the glass and the metal parts are relatively easy to clean and inspect. However, a small incidence of reactions

Fig. 1.—A 3 inch length of rubber tubing is slipped onto the Viscose tubing.

remained, and our suspicion centered on the rubber tubing because of the difficulties involved in the cleansing of tubing. New rubber tubing is covered with sulfur and other impurities which must be removed to render it pyrogen free. Rubber tubing which has been used for a blood or a plasma transfusion must be so thoroughly cleansed that there is complete removal of all residual protein matter from the lumen. One can never be certain that this has been accomplished.

Our method of preparing new and used rubber tubing is described in another publication.[6] This method of cleansing is drastic treatment to the rubber but was employed to reduce the possibility of febrile reactions. The effectiveness of this cleansing procedure was shown in a study by Zimmerman, Strauss and Laufman.[7] Five consecutive series of five hundred transfusions each were analyzed and showed progressive reduction in the incidence of transfusion reactions as the technic of the cleansing of rubber tubing and other equipment for intravenous injections was improved. The total incidence of pyrogenic reactions in the final series was 2.2 per cent, compared with 5.2 per cent in an earlier series.

The drastic cleansing of rubber eventually destroys its original elasticity. The original elasticity is what

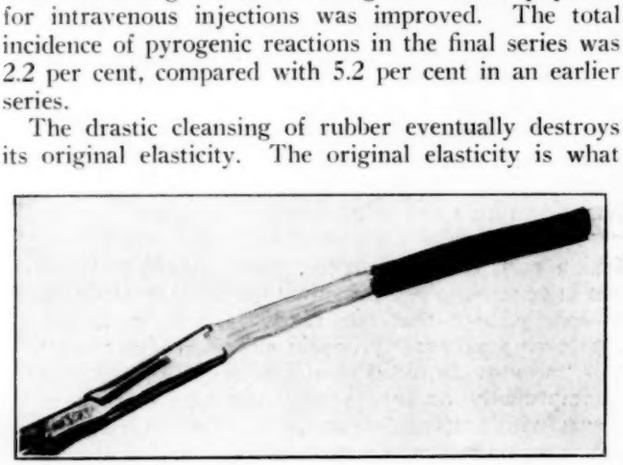

Fig. 2.—After moistening, the Viscose tubing is gently stretched with a hemostat.

makes rubber desirable for use in intravenous administration work. Once the tubing begins to deteriorate, fissures develop on the inside, and in this condition it can no longer be satisfactorily cleansed by any known procedure. It is hazardous to use old tubing for the administration of plasma, serum or blood, because the protein material cannot be completely removed. The residual protein material will then be subjected to autoclaving in sterilizing the administration set, and the coagulated protein even in minute amounts can cause severe reactions when a subsequent transfusion washes it into the blood stream. Old tubing may be used with relative safety when it is restricted solely to the administration of dextrose and saline solution and when protein material does not come in contact with it.

With these inherent defects of rubber tubing in mind, we sought a substitute. The regular Viscose tubing described by Hartman [8] was found by us to be fragile, difficult to handle and rather permeable to fluids. However, in our experience the heavy walled Viscose tubing has been free from these objections. The heavy walled tubing is far sturdier. The manufacturer impregnates the material with glycerin, which acts as a hygroscopic agent. The moisture content determines the suppleness of the Viscose tubing. Refrigerator storage is desirable for partially used rolls. The tubing is supplied in lengths of 1,500 feet, on spools, wrapped in wax paper, and at a cost so low that "one time use"

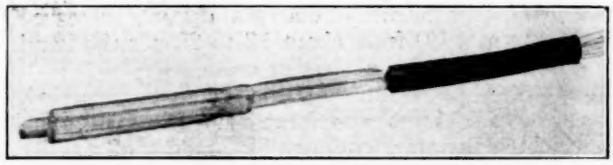

Fig. 3.—The expanded Viscose tubing is slipped onto the needle glass adapter ¾ inch.

Fig. 4.—The rubber tubing is slipped onto the joint and the clamp placed in position.

and discarding come to less than the cost of rubber, considering the time, labor and material used in maintaining rubber tubing. The drying effect from autoclaving can be minimized by making a compact package of each length of tubing to be sterilized and placing it within a glass tube measuring 25 by 100 mm. The glass tube inhibits vaporization of the moisture in the Viscose tubing during sterilization. In contrast to its brittleness when dry, Viscose tubing is quite pliable when wet and permits the required manipulation.

It was important to know whether the Viscose tubing was pyrogen free, impermeable to pyrogens and impermeable to bacteria.

## EXPERIMENTAL STUDIES

To determine whether the Viscose tubing was pyrogen free, 6 inch lengths were cut of every hundred feet from two rolls of Viscose tubing of 1,500 feet each. The specimens were cut into small pieces with sterile scissors and boiled in 200 cc. of pyrogen free distilled water for fifteen minutes. The water was filtered through filter paper, made isotonic with sodium chloride and subjected to a pyrogen test.[9] The pyrogen test was negative.

To ascertain whether pyrogens could diffuse through the wall of the Viscose tubing, the following tests were performed. A

6. Milzer, Albert: Laboratory Aspects of the Preparation and Biologic Control of Plasma, New York State J. Med., to be published.

7. Zimmerman, L. M.; Strauss, Anne Marie, and Laufman, Harold: Blood Transfusion Reactions: Their Causes and Prevention, Ann. Surg. **114:** 961 (Dec.) 1941.

8. Hartman, F. W.: Elimination of Rubber Tubing for Administration of Intravenous Solutions, Ann. Surg. **111:** 498, 1940.

9. United States Pharmacopeia, revision 12, pp. 606-607.

crystalline pyrogen [10] was used. The intravenous injection of 0.08 cc. (0.016 mg.) of this pyrogen into a dog weighing 13 Kg. caused a rise in rectal temperature of 1.9 degrees F. in two hours. To determine the effect of this pyrogen on rabbits, approximately 30 cc. of a 1 : 400 dilution of the pyrogen was injected into each of 5 rabbits. All the rabbits showed a positive response; the average rise in temperature was 2.3 degrees F. Then 10 cc. (0.2 mg.) of the concentrated pyrogen was placed in a length of Viscose tubing, and the tubing was suspended in 400 cc. of sterile nonpyrogenic isotonic solution of sodium chloride. Another flask containing 400 cc. of the same lot of saline solution served as a control. At the end of two hours at room temperature the Viscose tubing containing the pyrogen was removed, and the saline solution in each flask was subjected to a pyrogen test.[9] The saline solution in both flasks proved pyrogen free.

To determine whether bacteria could diffuse through Viscose tubing, the following test was performed: A diphtheroid isolated from contaminated human serum was inoculated in 15 cc. of Brewer's medium; the medium was then placed in a length of Viscose tubing and the tubing suspended in 400 cc. of sterile Brewer's medium. At the end of three weeks' incubation at 37.5 C. the medium surrounding the tubing was clear and sterile, whereas the medium in the Viscose tubing was turbid, indicating that bacterial growth was present in the tubing and that it had not penetrated through the tubing wall.

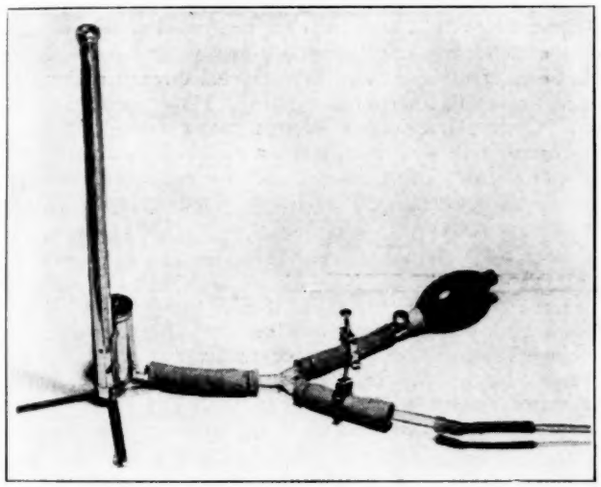

Fig. 5.—An airtight testing system uncovers leaky sections of tubing. After testing, suction is applied to return the tubing to its original flat shape.

## TECHNIC OF ASSEMBLY

The following technic has been developed for the use of Viscose tubing in assembling administration equipment:

1. Cut suitable lengths of tubing. Avoid sharp bends if the material is brittle.

2. Slip a 3 inch piece of rubber tubing over one end of the Viscose tubing, moving it down the Viscose tubing so that the terminal end of the Viscose tubing is exposed 2 inches (fig. 1).

3. Dip the exposed end of the Viscose tubing into pyrogen free distilled water for twenty to thirty seconds to permit wetting.

4. Insert a small hemostat into the lumen and enlarge the lumen by gentle spreading of the blades of the hemostat (fig. 2).

5. Moisten the end of a glass observation needle adapter in the distilled water, shake off excess water and slip ¾ inch of the expanded tubing over the glass fitting (fig. 3).

6. Allow the tubing to dry. This takes about ten minutes. The tubing will shrink and grip the glass. No adhesives are necessary.

10. BM 27 no. 2, supplied through the courtesy of Dr. Heinrich Necheles, director of the department of gastrointestinal research of the Michael Reese Hospital.

7. Slide the rubber tubing down over the glass part. Moistening the Viscose tubing and glass will facilitate this procedure. The rubber tubing acts as a guard at the junction of the Viscose tubing and the glass part; it also serves as a site for the metal clamp used for regulating the flow (fig. 4).

8. Each section of tubing must be examined for pinhole leaks. This is done by clamping off the free end of the Viscose tubing and inflating the tubing with a pressure bulb on a

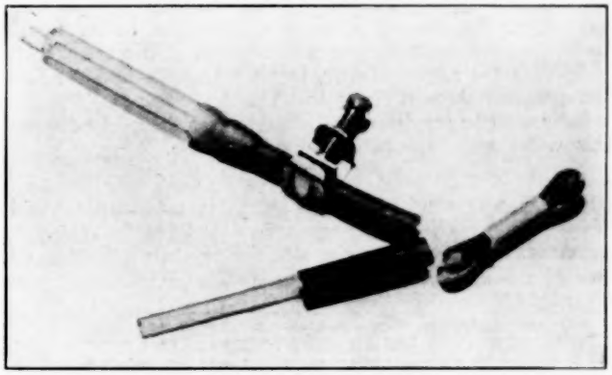

Fig. 6.—The Viscose tubing is folded on itself into a small package which can be slipped into a test tube. The other end of the tubing is ready for attachment to the second glass adapter.

manometer until the gage shows a pressure of 250 mm. of mercury. Close off the source of pressure and observe the gage. The reading should remain stationary. A rapid fall means that there is a leak in that section of tubing and that it should be discarded. A multiple testing manometer can be constructed simply (fig. 5).

9. With a suction bulb, completely evacuate the tubing until it is flat.

10. Fold the Viscose tubing on itself until it is a compact package about 2 inches long with the terminal end exposed about 3 inches. Wrap a band of paper around the tubing and fix it with a piece of Scotch tape. This will prevent the Viscose tubing from buckling in the autoclave (fig. 6).

11. Slip a 1½ inch piece of rubber tubing over the remaining free end of the Viscose tubing until 1½ inches of Viscose tubing is exposed. Dip the end in the distilled water, expand, and slip onto the glass filter chamber. Allow the Viscose tubing to dry, and slip the rubber guard onto the glass.

12. Complete assembly by connecting the filter to a glass Y tube (7 mm.), using a 2 inch piece of rubber tubing (⅛ by $\frac{3}{64}$). Slip a 3 inch piece of rubber tubing ($\frac{1}{16}$ by $\frac{3}{16}$) onto each

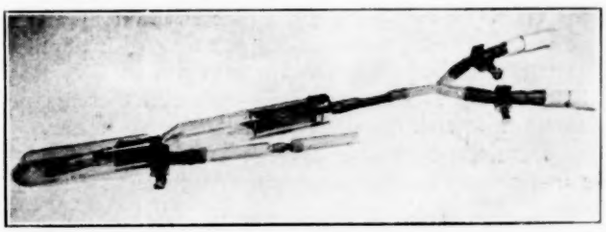

Fig. 7.—The assembly is completed and ready for wrapping and sterilization. Immediately before use the Viscose tubing will be soaked in water in the test tube to restore its suppleness.

end of the Y tube. Insert a glass bottle adapter in the free end of the rubber tubing and cover each adapter with unbleached muslin. Adjust shut-off clamps. Slip a glass tube 25 by 100 mm. over the Viscose tubing. This glass tube will prevent excessive drying of the Viscose tubing in the autoclave (fig. 7).

13. Wrap in two layers of gauze and then in flannel back canvas and sterilize at 15 pounds pressure for twenty minutes.

14. When the assembly is ready for use proceed as follows:

(*a*) Unwrap the sterile covering, remove the glass tube and remove the binding around the Viscose tubing. Aseptic technic is not necessary in handling the tubing.

(*b*) Fill the test tube three-fourths full with water (cold tap water may be used) and completely immerse the Viscose tubing in the water for one minute. The tubing will become soft and pliable.

(*c*) Close the shut-off clamp near the bottle adapter. Insert the adapter into the bottle and suspend the bottle on a rack at the proper height.

(*d*) The Viscose tubing should now be extended to its entire length. Avoid twisting the tubing.

(*e*) Open the shut-off clamp and allow the tubing to fill. Air bubbles can easily be seen and removed. Close the shut-off clamp near the needle adapter, insert the needle into the vein, then open the shut-off clamp to allow fluids to run. The flow of fluids must be regulated by the clamp near the needle adapter. This will prevent the tubing from collapsing.

15. After one time use the Viscose tubing is discarded.

16. The foregoing technic is used in combination with rubber tubing. The rubber tubing is used for a few inches of connection, and the Viscose tubing for sections requiring the bulk of tubing. Only new rubber tubing is used, and it is discarded after one time use.

## CLINICAL STUDIES

In order to determine the value of "one time use" Viscose tubing in reducing reactions in blood transfusions, we studied 600 transfusions, alternating rubber tubing and Viscose tubing. The results are recorded in table 1. This table shows a striking reduction in the number of pyrogenic reactions with Viscose tubing.

TABLE 1.—*Incidence of Pyrogenic Reactions with Rubber Tubing and with Viscose Tubing*

| | Transfusions | Pyrogenic Reactions | | Allergic | Total |
|---|---|---|---|---|---|
| | | Major | Minor | | |
| Rubber tubing..... | 300 | 2 (0.67%) | 5 (1.7%) | 1 (0.33%) | 8 (2.7%) |
| Viscose tubing..... | 300 | 0 (0.00%) | 0 (0.0%) | 2 (0.67%) | 2 (0.67%) |

TABLE 2.—*Analysis of Reactions with Viscose Tubing*

| Transfusions Made with Viscose Tubing | Pyrogenic Reactions | | Allergic | Total |
|---|---|---|---|---|
| | Major | Minor | | |
| 1,137 | 1 (0.09%) | 4 (0.3%) | 3 (0.25%) | 8 (0.64%) |

We classify as major a pyrogenic reaction in which there is a chill and a rise in temperature of 2 degrees or more above the pretransfusion level. If the elevation of temperature is less than 2 degrees and there is no chill or a mild one, the reaction is considered minor.

All infusions of whole blood, plasma and serum at this institution are now administered through Viscose tubing. The total reaction rate for all transfusions administered with Viscose tubing is recorded in table 2. The table shows a total of five pyrogenic reactions. The one major reaction occurred in a woman (group O) who received 500 cc. of citrated fresh blood. There was no untoward reaction at the time of the transfusion, and her temperature remained normal throughout the day. The following day, twenty-four hours after the transfusion, the patient complained of a chilly sensation and her temperature rose to 103.8 F. Forty-eight hours after the transfusion her temperature fell to 98.6 F.

The four minor pyrogenic reactions all occurred in a single patient, a 12 year old Negro girl (group A, Rh positive) suffering from sickle cell anemia. She had previously been in the hospital in July 1942 and at that time received six transfusions through rubber tubing. After three of these transfusions she experienced an immediate chill and a rise in temperature ranging from 1 to 2 degrees F. She was readmitted to the hospital in April 1943 and subsequently received four transfusions through Viscose tubing. A rise in temperature of 1 degree F. without chills occurred from three to six hours after each transfusion.

In 1941 Zimmerman and his associates [7] noted that febrile patients and patients suffering from leukemia showed a significantly higher incidence of untoward reactions than afebrile and surgical patients receiving citrated blood. He pointed out that patients suffering from septic diseases are particularly sensitive to minute and otherwise innocuous amounts of pyrogenic material.

An opportunity to use rubber tubing and Viscose tubing alternately in the same patient presented itself in 3 instances (2 of leukemia and 1 of ulcerative colitis):

CASE 1.—A girl aged 14 years (group A, Rh positive), suffering from ulcerative colitis, received fourteen transfusions of citrated blood of 250 cc. each over a period of four months. All the blood was homologous and was never over 72 hours old. Seven transfusions were administered through rubber tubing and seven through Viscose tubing. Three reactions developed following transfusions through rubber tubing. One was a pyrogenic type with a chill and a rise in temperature from 99.0 to 100.0 F. without chills. Following the transfusions with Viscose tubing there were no febrile reactions but there was one allergic reaction.

CASE 2.—A. J., a woman aged 43 (group O), suffering from monocytic leukemia, received fifteen transfusions of citrated blood of 500 cc. each over a period of eight weeks. All bloods given were less than seventy-two hours old. Eight transfusions were administered through rubber tubing and seven through Viscose tubing. Following the transfusions with rubber tubing two major pyrogenic reactions developed. The seven transfusions administered with Viscose tubing were uneventful.

CASE 3.—C. M., a man aged 63 (group O), suffering from chronic myelogenous leukemia, received fifteen transfusions at another hospital and had a history of several pyrogenic reactions. Three subsequent transfusions administered through Viscose tubing were uneventful.

## SUMMARY

The cleansing of rubber tubing to be used for intravenous administration of blood or blood protein is difficult. Incomplete cleansing of rubber tubing is believed to be a major cause of pyrogenic reactions.

Heavy walled Viscose tubing is sturdy, pyrogen free, impermeable to pyrogens, impermeable to bacteria and quite practical for one time use.

In a total of 1,137 blood transfusions given through Viscose tubing the incidence of pyrogenic reactions was 0.64 per cent. This is a material decrease from the reaction rate encountered with rubber tubing.

**Cardiovascular Signs of Emotion.**—The heart and the gastrointestinal tract are the most sensitive recorders of a disturbed emotional state. The intimate connections between the autonomic nervous system and the heart are so close as almost to justify the statement that cardiac rhythm and rate are a measure of the activity of the state of tension in the sympathetic and the parasympathetic systems.—Kraines, Samuel H.: The Therapy of the Neuroses and Psychoses, Philadelphia, Lea & Febiger, 1943.

# SULFAMERAZINE

## A CLINICAL STUDY OF ITS PHARMACODYNAMICS, THERAPEUTIC VALUE AND TOXICITY

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ST. LOUIS

As a result of the rather frequent occurrence of crystalluria and hematuria following the use of sulfathiazole and sulfadiazine, an effort has been made to find a sulfonamide derivative of comparable therapeutic potency with less tendency to produce crystals in the urinary tract. This problem is of special importance to our armed forces stationed in warm climates where it is exceedingly difficult to maintain a satisfactory urinary output.

Sulfamerazine (2-sulfanilamido-4-methylpyrimidine) has been investigated because of its greater solubility as compared to other pyrimidine derivatives.[1] Welch and his co-workers[2] found that sulfamerazine and its acetyl derivative were approximately 20 per cent more soluble than the respective forms of sulfadiazine in both water and urine. Additional studies by Welch and his co-workers,[2] Goodwin and his co-workers,[3] and Murphy and his co-workers[4] indicated that sulfamerazine was more rapidly and completely absorbed from the gastrointestinal tract and also that the drug was more slowly excreted. These observations suggested that satisfactory blood levels might be attained with smaller doses of sulfamerazine and that the interval between doses might be lengthened. During the past four months 103 patients have been treated with sulfamerazine[5] at the Barnes Hospital and the St. Louis City Isolation Hospital. The therapeutic results and toxic reactions observed constitute the subject of this paper.

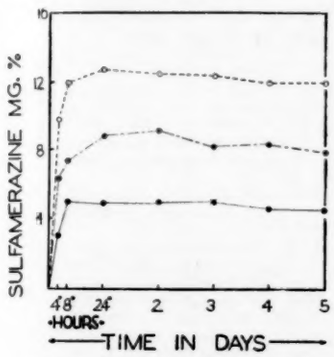


Chart 1.—Absorption curve following 4 Gm. of sulfamerazine given orally with maintenance dose of 1 Gm. every eight hours. Blood levels are expressed as mg. % of "free" sulfamerazine. Curve at top, maximum; at bottom, minimum; in center, average.

From the Department of Medicine, Washington University School of Medicine.

This study was carried out at the suggestion of the Chemotherapy Committee of the National Research Council.

The essential part of the work was done by the staffs of Barnes Hospital and the St. Louis City Isolation Hospital.

1. Roblin, R. O.; Williams, J. H.; Winney, P. S., and English, J. P.: Chemotherapy: II. Some Sulfanilamido Heterocycles, J. Am. Chem. Soc. **62**: 2002, 1940. Caldwell, W. T.; Kornfeld, E. C., and Donnell, C. K.: Substituted 2-Sulfanilamidopyrimidines, ibid. **63**: 2188, 1941. Sprague, J. M.; Kissonger, L. W., and Lincoln, R. M.: Sulfonamido Derivatives of Pyrimidines, ibid. **63**: 3028, 1941.

2. Welch, A. D.; Mattis, P. A.; Latven, A. R.; Benson, W. M., and Shiels, E. H.: Sulfamerazine: Absorption, Excretion and Toxicity, Pharmacological Laboratories, Medical Research Division, Sharpe and Dohme, Inc.; Sulfamerazine: 1. A Comparison of Sulfamerazine with Sulfadiazine on the Basis of Absorption, Excretion and Toxicity, J. Pharmacol. & Exper. Therap. **77**: 357, 1943.

3. Goodwin, R. A.; Peterson, O. L., and Finland, Maxwell: Absorption and Excretion of Sulfamethyldiazine in Human Subjects, Proc. Soc. Exper. Biol. & Med. **51**: 262, 1942.

4. Murphy, F. D.; Clark, J. K., and Flippin, H. F.: Studies on 2-Sulfanilamido-4-Methyl-Pyrimidine (Sulfamerazine, Sulfamethyldiazine) in Man: 1. Absorption, Distribution and Excretion, Am. J. M. Sc. **205**: 717, 1943.

5. Dr. William A. Feirer of Sharpe & Dohme, Inc., supplied the sulfamerazine used in this study.

### PROCEDURE

All patients were accepted for treatment provided other sulfonamides had not been previously administered during the current illness. In general, the drug was administered as follows:

An initial dose of 4 Gm. was given (orally when feasible) and maintainence doses of 1 Gm. every eight hours were given thereafter. For severely ill patients this dosage scheme was modified and initial doses up to 8 Gm. and maintenance doses of 2 Gm. every eight hours were often given. In addition, if blood concentrations did not attain desired levels supplementary doses were occasionally administered. Alkalis were not given to any patient. It was planned to force fluids to 3,000 cc. in twenty-four hours in all cases in an effort to obtain a urinary output of 1,000 cc. or more in twenty-four hours. Because of the shortage of hospital personnel, it was not possible to control the fluid intake adequately in every case, particularly during epidemic periods, and in certain instances the fluid intake fell below the desired level. Blood concentrations were measured at least every twenty-four hours at a time just preceding the eight hour maintenance dose. Determinations of the sulfamerazine concentration were done by the method of Bratton and Marshall.[6] All figures quoted are values for free sulfamerizine in whole blood. Urinalyses were performed daily during treatment, the microscopic examination being done as soon as possible after the patient voided. In some instances specimens remained at room temperature for one or two hours before being examined. Red blood cell counts, hemoglobin determinations and white blood cell counts were made at least every three days during treatment.

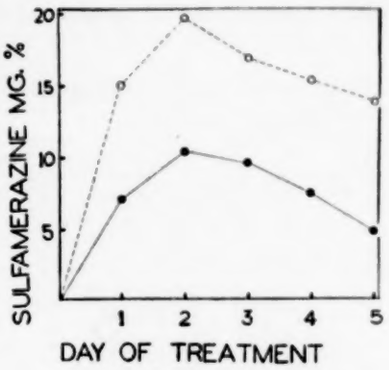


Chart 2.—Average of blood and spinal fluid free sulfamerazine levels in 19 cases of meningococcic meningitis. Curve at top, blood; at bottom, cerebrospinal fluid.

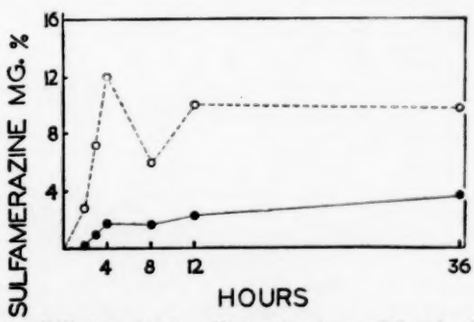


Chart 3.—Diffusion of free sulfamerazine into uninfected spinal fluid following oral administration of 4 Gm. of sulfamerazine. Curve at top, blood; at bottom, cerebrospinal fluid. The 4 and 36 hour figures are the average of two sets of observations. Other values represent individual instances from different patients.

Culture mediums employed were beef or horse infusion broth and agar with 1 per cent Bacto-peptone, 1 per cent dextrose and 5 mg. of para-aminobenzoic acid per hundred cubic centimeters. Spinal fluid cultures were

6. Bratton, A. C., and Marshall, E. K.: A New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128**: 537, 1939.

made on beef or horse infusion blood agar slants. Cultures for meningococci were grown in 10 per cent carbon dioxide. In many instances additional samples of spinal fluid were inoculated on the chorioallantoic membrane of the chick embryo.[7]

### PHARMACODYNAMICS

Absorption of the drug was followed closely in the first twelve patients treated (chart 1). The resulting curves are similar to those obtained by Welch [2] and by Goodwin.[3] Both rapid absorption and maintenance of high blood concentrations, with the drug administered every eight hours, are well demonstrated.

During the course of the study the diffusion of sulfamerazine into the spinal fluid was observed (chart 2), care being taken to use 1 per cent metycaine [8] as a local anesthetic. In 19 cases of meningitis the spinal fluid concentrations averaged 49 per cent of the blood concentrations during the period of treatment. A few observations have been made on the relative concentrations of blood and spinal fluid shortly after administration of the drug to patients without meningitis who had lumbar punctures for various reasons. These are plotted in chart 3 and suggest that a considerable lag occurs in the diffusion of the drug into the uninfected spinal fluid. In several instances simultaneous blood and pleural fluid concentrations were observed to show approximately the same levels in the fluid and the blood (examples: blood 6.4, pleural fluid 6.4; blood 6.7, pleural fluid 6.8; blood 6.3, pleural fluid 7.9).

TABLE 1.—*Meningococcic Infections Treated with Sulfamerazine*

| Case No. | Age, Sex | Day of Disease * | Severity of Infection | Cultures: Blood | Cultures: Spinal Fluid | Duration of Treatment, Days | Total Amount Drug, Gm. | Drug Concentration †: Blood: 24 Hr. | Blood: Maximum | Blood: Average | Cerebrospinal Fluid: 24 Hr. | Cerebrospinal Fluid: Maximum | Cerebrospinal Fluid: Average | Therapeutic Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 I | 6 ♂ | 3 | 102 F., petechiae, CSF 7,000 cells | + | + | 12 | 38 | 21.5 | 21.5 | 11.2 | 10.5 | 10.5 | 5.7 | Cultures negative after first day; temperature normal 8th day; uneventful recovery |
| 5 I | 14 ♀ | 2 | 101 F., petechiae, rheumatic heart disease, CSF 12,000 cells | + | + | 10 | 62 | 18.5 | 23 | 18.4 | 9 | 12 | 9.4 | Cultures negative after first day; temperature normal 8th day; uneventful recovery |
| 6 I | 24 ♀ | 3 | 102 F., petechiae, 8 mos. pregnant CSF 3,950 cells | — | —‡ | 7 | 42 | 15 | 25.5 | 16.6 | 6 | 14 | 10.6 | Temperature normal in 12 hours; uneventful recovery |
| 9 I | 7 ♀ | 2 | 101.2 F., petechiae, CSF 25 cells | + | — | 6 | 20 | 18 | 18 | 10.7 | .... | .... | .... | Temperature normal on 4th day; blood culture positive on 4th day; uneventful recovery |
| 12 I | 17 ♀ | 3 | 103 F., petechiae, comatose, CSF 19,000 cells | — | + | 10 | 38 | 18.8 | 18.8 | 13.2 | 8.4 | 8.4 | 6.5 | Culture negative after first day; temperature normal on 8th day; uneventful recovery |
| 13 I | 24 ♂ | 3 | 103.8 F., epileptic, CSF 25,000 cells | — | + | 9 | 34 | 17.2 | 17.2 | 7.5 | 8.6 | 8.6 | 5.1 | Culture positive on 2d day of treatment; temperature normal on 5th day; uneventful recovery |
| 15 I | 2 ♂ | 2 | 100.6 F., severe, CSF 22,000 cells | + | + | 11 | 46.5 | 6.5 | 30 | 14.2 | 4.3 | 19.5 | 8.1 | CSF positive on 3d day of treatment; temperature normal on 12th day; uneventful recovery |
| 16 I | 16 ♂ | 3 | 102 F., petechiae, stuporous, CSF 38,000 cells | — | +§ | 12 | 61.5 | 10.5 | 12 | 9 | 4.6 | 7 | 4.8 | Temperature normal on 12th day; uneventful recovery |
| 20 I | 12 ♀ | 2 | 100.4 F., petechiae, stuporous, CSF 12,500 cells | — | + | 3 | 20 | 17.8 | 18.8 | 16.7 | 10 | 10 | 8.5 | Hematuria; temperature normal on 8th day; uneventful recovery |
| 21 I | 38 ♂ | ? | 103 F., coma, iritis, CSF 3,100 cells | — | + | 8 | 52 | 21 | 21 | 16.6 | 13 | 13 | 12.2 | Temperature normal 4th day; iritis subsided; uneventful recovery |
| 22 I | 18 ♂ | 2 | 104 F., petechiae, maniacal, CSF 3,300 cells | + | ?‖ | 14 | 89 | 15.7 | 27 | 19.5 | 7.5 | 15.8 | 12.9 | Temperature normal 15th day; uneventful recovery |
| 23 I | 20 ♀ | 4 | 103 F., petechiae, CSF 160 cells | + | + | 9 | 60 | 13 | 25 | 18.8 | 8.3 | 15.2 | 11.5 | CSF positive on 2d day; temperature normal 7th day; uneventful recovery |
| 24 I | 74 ♂ | 1 | 101.4 F., irrational, ecchymoses, CSF 6,150 cells | ?¶ | ?‖ | 5 | 41 | 37.5 | 37.5 | 24.2 | 20 | 20 | 17 | Onset 2 days after transurethral resection; uneventful recovery |
| 25 I | 52 ♂ | ? | 101 F., petechiae, mentally dulled, hemiplegic, CSF 9,500 cells | ?¶ | +§ | 15 | 120 | 12.5 | 29 | 15.5 | 8 | 17.5 | 8.2 | Temperature septic throughout; CSF positive on 2d and 5th days; developed pneumonia and died on sulfapyridine; autopsy performed |
| 26 I | 20 ♀ | 2 | 103.2 F., drowsy, CSF 12,000 cells | + | + | 8 | 50 | 21 | 21 | 16.7 | 8.5 | 8.5 | 8.1 | Temperature normal 6th day; uneventful recovery |
| 27 I | 65 ♂ | ? | 103 F., stuporous, hypertension, CSF 19,200 cells | 0 | + | 4 | 22 | 13.6 | 15.4 | 13.7 | 5.4 | 7.5 | 9.6 | CSF xanthrochromic; died on 4th day; no autopsy obtained |
| 28 I | 14 ♂ | 2 | 103.4 F., petechiae, irrational, CSF 3,760 cells | + | + | 9 | 44 | 19.4 | 22 | 16.8 | 4 | 6.5 | 5.7 | Temperature normal 13th day—drug fever with rash; uneventful recovery |
| 29 I | 17 ♀ | 1 | 102.4 F., CSF 17,500 cells | — | +§ | 5 | 35 | 17 | 18.8 | 17.4 | 7.5 | 10.4 | 8.6 | Temperature normal 7th day; hematuria; uneventful recovery |
| 30 I | 25 ♀ | 4 | 100 F., petechiae, CSF 13,000 cells | — | —‡ | 7 | 41 | 12 | 21 | 14.9 | 7 | 7 | 5.8 | Swollen wrist on 5th day, subsided; uneventful recovery |

### THERAPEUTIC RESULTS

(*a*) *Meningococcic Infections.*—Thirty-seven patients with meningococcic meningitis were treated as outlined in table 1.[9] The therapeutic results were, on the whole, satisfactory. Most of the patients improved rapidly under treatment and all but 5 recovered. There were 3 pregnant women (6 I, 31 I, 42 I) who recovered without apparent harm to the fetus. A single case

7. Through the courtesy of Dr. Russell Blattner. To be published.
8. Gamma-(2-methylpiperidino)-propyl Benzoate Hydrochloride, Lilly.

9. Blood and spinal fluid levels are charted as follows: (1) the value attained twenty-four hours after the onset of treatment, (2) the maximum level reached and (3) the average level observed during the period of therapy. Case numbers are accompanied by the letters I and B, indicating the hospital in which the patient was treated, i. e. St. Louis City Isolation Hospital or Barnes Hospital.

(55 B) was complicated by diabetic acidosis and the patient survived. In one instance (21 I) a complicating iritis subsided without a residual lesion. A man aged 74 (24 I) developed the disease on the second postoperative day following a transurethral prostatic resection, and under sulfamerazine therapy his recovery was uneventful.

On a number of occasions a low grade fever persisted for several days after the patient seemed to have

(*b*) *Pneumococcic Infections.*—Seventeen patients with pneumococcic infection were treated as outlined in table 2. The results were uniformly good in the pneumonic infections, but there were only 2 patients with bacteremia. Patient 17 I with meningitis and bacteremia died thirteen hours after being admitted to the hospital.

(*c*) *Streptococcic Infections.*—Fifteen patients with streptococcic infection were included in the present

TABLE 1.—*Meningococcic Infections Treated with Sulfamerazine—Continued*

| Case No. | Age, Sex | Day of Disease * | Severity of Infection | Cultures: Blood | Cultures: Spinal Fluid | Duration of Treatment, Days | Total Amount Drug, Gm. | Drug Concentration †: Blood: 24 Hr. | Blood: Maximum | Blood: Average | Cerebrospinal Fluid: 24 Hr. | Cerebrospinal Fluid: Maximum | Cerebrospinal Fluid: Average | Therapeutic Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 31 I | 19 ♀ | 1 | 100 F., lethargic, pregnant, CSF 1,300 cells | + | + | 6 | 36 | 21.6 | 21.6 | 16.3 | .... | .... | .... | Temperature normal 4th day; hematuria; uneventful recovery |
| 32 I | 67 ♀ | 2 | 104.6 F., stupor, hypertension, CSF 56,000 cells | + | + | 2 | 12 | 9 | .... | .... | .... | .... | .... | NPN 65 at admission with 4+ albumin and red blood cells in urine; died in 32 hours; no autopsy |
| 33 I | 15 ♂ | 1 | 99.8 F., CSF 5,300 cells | — | —‡ | 6 | 32 | 15.4 | 22.5 | 19.8 | .... | .... | .... | Temperature normal 2d day; uneventful recovery |
| 34 I | 21 ♀ | 1 | 102.8 F., lethargic, petechiae, CSF 380 cells, fluid turbid from bacteria | + | + | 3 | 18 | 14 | 21 | 17.2 | .... | .... | .... | Changed to sulfanilamide on 4th day because of rash; CSF positive on 3d and 7th days; eventually recovered |
| 35 I | 24 ♂ | 3 | 100 F., lethargic, petechiae, arthritis, CSF 5,400 cells | — | + | 18 | 142 | 7.8 | 24 | 8.6 | 10.5 | .... | .... | CSF positive on 6th day; joints subsided slowly; recovered |
| 36 I | 60 ♂ | ? | 102 F., coma, petechiae, CSF 7,600 cells | — | + | 1 | 12.3 | 16.2 | .... | .... | .... | .... | .... | Died after 22 hours; no autopsy |
| 37 I | 14 ♂ | 1 | 101.2 F., stuporous, petechiae, CSF 18,450 cells | — | + | 7 | 43.5 | 11.4 | 19.3 | 11.6 | .... | .... | .... | Temperature normal 5th day; uneventful recovery |
| 39 I | 34 ♂ | 2 | 100 F., delirious petechiae, CSF 35,200 cells | — | + | 8 | 52 | 9.5 | 15.8 | 9.9 | .... | .... | .... | Received 50,000 units of meningococcus antitoxin; temperature normal 5th day; uneventful recovery |
| 40 I | 56 ♂ | 2 | 100.4 F., CSF 4,320 cells | — | —¶ | 7 | 41 | 9 | 17.5 | 12.1 | .... | .... | .... | Temperature normal 2d day; uneventful recovery |
| 41 I | 35 ♀ | 2 | 100.2 F., stuporous, CSF 1,600 cells | — | + | 6 | 41 | 12 | 17.2 | 13.3 | 7.8 | .... | .... | Temperature normal 4th day; uneventful recovery |
| 42 I | 32 ♀ | 2 | 98.6 F., petechiae, pregnant, CSF 17,250 cells | — | + | 8 | 46 | 13.5 | 30 | 16.2 | .... | .... | .... | Received 50,000 units of meningococcus antitoxin; hematuria; uneventful recovery |
| 45 I | 15 ♀ | 2 | 102.6 F., stuporous, CSF 11,200 cells | — | —‡ | 10 | 54 | 12 | 15 | 11.8 | .... | .... | .... | Temperature normal 7th day; hematuria; uneventful recovery |
| 46 I | 21 ♀ | 2 | 100 F., lethargic, petechiae, CSF 27,500 cells | — | + | 5 | 38 | 15 | 15 | 11.1 | .... | .... | .... | Temperature normal 11th day; hematuria; uneventful recovery |
| 47 I | 14 ♂ | 1 | 102.6 F., petechiae, CSF 11,800 cells | — | —‡ | 7 | 38 | 16.4 | 23 | 19.7 | .... | .... | .... | Temperature normal 4th day; hematuria; uneventful recovery |
| 48 I | 15 ♂ | 2 | 101.4 F., lethargic, petechiae, CSF 8,100 cells | + | + | 10 | 61 | 21 | 21 | 17.9 | .... | .... | .... | ? Drug fever; uneventful recovery |
| 49 I | 23 ♀ | 4 | 103.8 F., mentally dulled, CSF 30,000 cells | — | + | 9 | 56 | 23.5 | 23.5 | 19.2 | .... | .... | .... | Temperature normal 5th day; uneventful recovery |
| 41 B | 62 ♀ | 2 | 103.4 F., coma, petechiae, CSF 1,750 cells | — | + | 4 | 10.5 | 19 | 20.2 | 15.6 | 10 | 10 | 9.3 | NPN 60 at admission; received 60 cc. of meningococcus antiserum; CSF became sterile; died in uremia; autopsy performed |
| 55 B | 52 ♂ | 2 | 104.4 F., coma, diabetic acidosis, CSF 14,850 cells | + | + | 6 | 37 | 10.4 | 14.5 | 10.5 | .... | .... | .... | Changed to sulfadiazine because of ? drug fever; recovered slowly; some possible neurologic residual |

* Day of disease therapy was begun.
† 24 hour, level attained at end of 24 hours of treatment; maximum, highest level attained during treatment; average, average of all levels during treatment.
‡ Smear positive for gram-negative diplococci.
§ Culture positive on chorioallantoic membrane of cheek embryo only.
‖ Smear positive for gram-negative diplococci, culture contaminated.
¶ Culture contaminated.
# Smear negative.

otherwise recovered completely (examples: 15 I, 16 I). Cultures of blood or spinal fluid remained positive for several days in a few instances (9 I, 15 I, 25 I, 34 I, 35 I). The only possible residual lesion was observed in patient 55 B, who has an increased left ankle jerk and is still under observation.

Five patients in the group (25 I, 27 I, 32 I, 36 I and 41 B), all of whom were elderly with complicating medical conditions such as hypertension, hemiplegia and kidney insufficiency, failed to survive. The case fatality rate for the group of 37 patients was 13.5 per cent.

series (table 3). Although these were not severe infections (except 45 B) the response to treatment was satisfactory. In 1 instance (33 B) an abscess formed which contained sterile thin pus. Patient 45 B had severe uncontrolled diabetes with advanced gangrene of one foot. Blood cultures contained 8 to 12 organisms per cubic centimeter at the onset of treatment, and subsequent cultures showed no growth. The patient died on the third day of treatment.

(*d*) *Urinary Tract Infections.*—Four patients with urinary tract infections were treated as outlined in

table 4. Results were uniformly satisfactory; however, none of the patients had bacteremia.

(*e*) *Miscellaneous Infections.*—Thirty patients with miscellaneous diseases including gonococcic and staphylococcic infections also were treated, and the results obtained were comparable to those observed with sulfadiazine therapy.

Drug fever with morbilliform rash was observed twice (28 I, 34 I) (1.9 per cent). The rash was similar to that seen with other sulfonamides.

Neuropathologic changes, agranulocytosis, anemia, nausea and vomiting were not observed in this series.

TABLE 2.—*Pneumococcic Infections Treated with Sulfamerazine*

| Case No. | Age | Sex | Day of Disease * | Number of Lobe | Type of Pneumococcus | Blood Culture | Severity of Disease | Duration of Treatment, Days | Total Amount Drug, Gm. | Blood Concentration 24 Hr. | Blood Concentration Maximum | Blood Concentration Average | Therapeutic Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 B | 25 | ♂ | 3 | I | I | — | Moderate | 5 | 19 | 9.8 | 9.8 | 7.8 | ? Drug fever; excellent |
| 2 B | 21 | ♀ | 3 | I | V | — | Moderate | 15 | 52 | 8.4 | 10.7 | 8.5 | Excellent |
| 6 B | 51 | ♂ | 16 | Broncho | IX | — | Chronic lymphatic leukemia | 6 | 20 | 9.5 | 12.3 | 11.1 | Good |
| 7 B | 69 | ♂ | 10 | Broncho | ?† | — | Bronchial asthma | 6 | 20 | 6.6 | 11.8 | 9.8 | Good |
| 8 B | 49 | ♀ | 3 | I | VI | — | Bronchial asthma | 12 | 39 | 13.2 | 13.2 | 10.4 | Excellent |
| 9 B | 56 | ♂ | ?1 | Broncho | ?† | — | Cardiac failure | 13 | 44 | 6.5 | 6.5 | 5.3 | Course not altered |
| 10 B | 50 | ♀ | 1 | I | VI | — | Moderate | 8 | 26 | 11 | 11 | 6.5 | Excellent |
| 16 B | 20 | ♂ | 1 | I | I | + | Severe | 9 | 27 | 8.2 | 8.4 | 6.6 | Hematuria; excellent |
| 19 B | 49 | ♂ | ? | Broncho | ?† | — | Emphysema and chronic bronchitis | 9 | 32 | 6.7 | 9.1 | 5.6 | Good |
| 20 B | 57 | ♂ | 1 | I | XXVIII | — | Moderate | 7 | 24 | 7.6 | 7.9 | 5.6 | Excellent |
| 22 B | 73 | ♂ | ? | Broncho | ?† | — | Bronchial asthma | 5 | 19 | 13.3 | 13.3 | 10.4 | Good |
| 34 B | 35 | ♀ | 4 | I | I | + | Bronchial asthma | 6 | 22 | 12.1 | 12.1 | 7.4 | Excellent |
| 37 B | 53 | ♂ | 2 | Broncho | IV | — | Hemiplegia | 6 | 23 | 7.3 | 10.7 | 9.0 | Excellent |
| 58 B | 56 | ♂ | 5 | II | I, XIV | — | Cardiac failure, jaundice | 19 | 40 | 17.5 | 22.3 | 13.3 | ? Drug fever; received 300,000 units of type I rabbit serum; recovered slowly |
| 53 B | 69 | ♀ | 1 | I | ?† | — | ? Pulmonary infaret | 11 | 31 | 14.6 | 16.1 | 13.1 | ? Drug fever; good |
| 14 I | 12 | ♀ | 2 | I | ?† | — | Meningismus | 7 | 24 | 12 | 14.4 | 12.3 | Excellent |
| 17 I | 54 | ♀ | 2 | Meningitis | XIX | + | Comatose | 13 | 14 | .... | 14.4 | 12.3 | Died in 13 hours; no autopsy |

* Day of disease treatment was begun. † Pneumococcus isolated but not typable.

TABLE 3.—*Beta-Hemolytic Streptococcus Infections Treated with Sulfamerazine*

| Case No. | Age | Sex | Diagnosis | Day of Disease * | Severity | Local Cultures † | Blood Cultures † | Duration of Treatment, Days | Total Amount Drug, Gm. | Blood Concentration 24 Hr. | Blood Concentration Maximum | Blood Concentration Average | Therapeutic Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3 B | 22 | ♀ | Pharyngitis | 2 | Moderate | + | — | 6 | 22 | 8.4 | 9 | 8.1 | Excellent |
| 12 B | 23 | ♀ | Tonsillitis, peritonsillar abscess | 4 | Severe | + | — | 8 | 26 | 11.1 | 13.3 | 11.2 | Excellent |
| 15 B | 34 | ♀ | Pharyngitis | 2 | Severe | + | — | 3 | 13 | 10.4 | 10.4 | 8.3 | Excellent |
| 30 B | 24 | ♂ | Pharyngitis | 3 | Severe | + | — | 2 | 9 | 10.8 | 12.6 | 11.7 | Excellent |
| 42 B | 20 | ♀ | Pharyngitis | 2 | Severe | + | — | 3 | 13 | 16.6 | 16.6 | 16.2 | Excellent |
| 11 B | 41 | ♂ | Erysipelas | 1 | Moderate, thrombophlebitis | 0 | — | 6 | 21 | 6.9 | 6.9 | 6.2 | Good |
| 33 B ‡ | 41 | ♂ | Erysipelas, abscess | 4 | Severe, thrombophlebitis | — | — | 14 | 28 | 6.6 | 9.4 | 5.7 | Good; sterile abscess |
| 18 I | 64 | ♂ | Erysipelas | 1 | Moderate | 0 | 0 | 7 | 22 | 8.5 | 14.2 | 9.8 | Maniacal on 3d and 4th days; lesion cleared rapidly |
| 19 I | 84 | ♂ | Erysipelas | ? | Mild | 0 | 0 | 8 | 23 | 9 | 9 | 6.2 | Excellent |
| 38 I | 74 | ♂ | Erysipelas | 3 | Mild | 0 | 0 | 8 | 25 | 15 | 15 | 12.9 | Lesion cleared rapidly; temperature normal 8th day |
| 43 I | 40 | ♀ | Erysipelas | 2 | Mild | 0 | 0 | 7 | 20 | 11.4 | 11.4 | 6.9 | Excellent |
| 44 I | 70 | ♂ | Erysipelas | 2 | Moderate | 0 | 0 | 7 | 21 | 7.5 | 7.5 | 5.0 | Excellent |
| 50 I | 30 | ♂ | Erysipelas | 2 | Severe | 0 | 0 | 6 | 19 | 12.5 | 14.4 | 12.5 | Excellent |
| 11 I | 14 | ♂ | Scarlet fever | 2 | Moderate | 0 | 0 | 8 | 25 | 14 | 14.7 | 12.3 | Excellent |
| 45 B | 73 | ♂ | Septicemia | ? | Severe, diabetic gangrene | 0 | + | 3 | 13 | 12.6 | 14.9 | 13.5 | Died; blood culture negative before death |

* Day of disease treatment was begun. † + = culture positive, — = culture negative, 0 = culture not obtained.
‡ Same as patient 11 B.

## TOXICITY

Drug fever was noted in 6 instances (1 B, 27 B, 53 B, 55 B, 58 B, 48 I), an incidence of 5.8 per cent. This reaction was not unlike that observed with other sulfonamides as to severity, time of appearance and response to withdrawal of drug.

Although animal experiments [2] had not shown notable neuropathologic changes, neurologic symptoms and signs were carefully watched for because of the experience reported with sulfamethylthiazole, a similar methyl derivative.

Crystalluria without hematuria was noted in 7 cases (4 B, 6 B, 19 B, 2 I, 4 I, 23 I, 37 I), an incidence of 6.8 per cent. None of the patients complained of symp-

toms, and the crystals could be seen only microscopically. Eight other patients showed crystalluria in urine specimens that were exposed to room temperature for one to two hours, but these results were discarded when fresh urines were found to be free of crystals. In every instance in which fresh urines were not checked to confirm the presence of crystalluria, the case was included as one showing crystalluria. The mere fact that crystals often appeared at room temperature soon after voiding suggests that the urine approaches saturation with sulfamerazine and its acetyl derivatives. Attempts to relate the presence of crystals to the blood concentration failed to reveal a correlation.

One patient (25 I, table 1) had no crystals or red blood cells in daily urine samples but at autopsy was found to have concretions of sulfonamide crystals in parable to that obtained with a larger fluid intake in a hot climate.

Hematuria was observed in 9 instances (8.7 per cent), (table 5). In 3 of the 9 cases the hematuria was grossly visible and in the others the red blood cells varied from "many" to "occasional" (47 I) per high power field in the centrifuged specimen. Crystalluria was observed at some time during treatment in 3 of the 9. Attempts to correlate the occurrence of hematuria with blood levels have shown no apparent relationship. Four of the 9 patients had petechiae in the skin.

Patient 29 I was menstruating at the time hematuria was reported. Catheterized specimens contained red blood cells, but the possibility of menstrual contamination is not excluded, since a two glass technic was

TABLE 4.—*Bacillus Coli Infections Treated with Sulfamerazine*

| Case No. | Age | Sex | Diagnosis | Urine Culture | Urinary WBC/HPField, Cent | Duration of Treatment, Days | Total Amount Drug, Gm. | Blood Concentrations | | | Therapeutic Result |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | 24 Hr. | Maximum | Average | |
| 38 B | 62 | ♀ | Pyelitis, ? brucellosis | + | 10+ | 9 | 25 | 11.3 | 19.3 | 15 | Excellent |
| 43 B | 64 | ♂ | Cystitis, carcinoma of prostate | + | Occasional clumps | 7 | 24 | .... | 4 | 3.6 | Culture negative before death |
| 49 B | 34 | ♀ | Cystitis, cystocele | + | "Many" | 5 | 17 | 15.8 | 15.8 | 15.5 | Good |
| 59 B | 69 | ♂ | Cystitis, coronary artery disease | + | 200 | 4 | 13 | .... | 8.6 | .... | Good |

TABLE 5.—*Cases of Hematuria Observed During Sulfamerazine Treatment*

| Case No. | Age | Sex | Petechiae | Day of Treatment * | Intake,† Cc. per 24 Hr. | Output,† Cc. per 24 Hr. | Blood Concentration | | | Nonprotein Nitrogen | Day of Crystalluria § | Severity | Duration in Days ‖ | Result |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | Hematuria | Maximum | Average ‡ | | | | | |
| 20 I | 12 | ♀ | + | 3 | 1,730 | Incontinent | 13.5 | 18.8 | 16.7 | 32 | 0 | Gross | 3 | Subsided promptly |
| 29 I | 17 | ♀ | — | 5 | 2,140 | 1,300 | 18.8 | 18.8 | 17.4 | — | 0 | Micro. | 3 | Subsided promptly (menstruating) |
| 31 I | 19 | ♀ | — | 6 | 1,875 | 715+ | 14 | 21.6 | 16.3 | — | 4 | Gross | 3 | Subsided promptly |
| 42 I | 32 | ♀ | + | 6 | 2,500 | 720+ | 13.5 | 30 | 16.2 | 18 | 3 | Micro. | 4 | Pregnant; albumin 8th day; subsided |
| 45 I | 15 | ♀ | — | 8 | 2,300 | 1,470 | 11.5 | 15 | 11.8 | — | 5 | Micro. | 1 | Subsided promptly |
| 46 I | 21 | ♀ | + | 4 | 2,360 | 2,100 | 7 | 15 | 11.1 | 24 | 0 | Gross | 5 | Subsided promptly |
| 47 I | 14 | ♂ | + | 6 | 1,910+ | 1,480 | 21.5 | 23 | 19.7 | — | 0 | Micro. | 2 | Subsided promptly |
| 16 B | 20 | ♂ | — | 7 | 3,170 | 2,170 | 3.8 | 8.4 | 6.6 | — | 0 | Micro. | 4 | Subsided promptly |
| 36 B | 32 | ♂ | — | 13 | 2,630 | 2,092 | 9.7 | 16.2 | 13.6 | 19 | 0 | Micro. | 1 | Subsided promptly |

* Day of treatment hematuria first appeared.
† Average of 3 days preceding onset of hematuria.
‡ Blood concentration: at time of hematuria, maximum level before hematuria, average level during therapy.
§ Day of treatment crystals were first seen. ‖ Duration of hematuria.

both ureters. Since the patient had received sulfapyridine following cessation of sulfamerazine treatment, the identity of the crystals was open to question. Samples were sent to Sharpe and Dohme [10] and were identified as acetyl-sulfamerazine. The daily fluid intake averaged 1,800 + cc. and the urinary output 850 + cc. during the period of sulfamerazine treatment. Blood nonprotein nitrogen was not measured at any time, as urinary complications were not suspected. Urinary suppression was not noted terminally, but the output was not accurately known because of urinary incontinence. This patient received large doses of sulfamerazine, averaging 8 Gm. in twenty-four hours for fifteen days, and the blood concentration reached 29 mg. per hundred cubic centimeters on one occasion. It is felt that the crystalline deposits were due to an inadequate intake of fluid, but the urinary output might be quite com-

10. Through courtesy of Dr. Earl L. Burbidge Jr.

not employed. It is of interest that patient 36 B had a bloody stool on the day hematuria was reported; no subsequent episodes of hemorrhage occurred.

None of the patients developed nitrogen retention, urinary suppression or other evidence of kidney impairment. Symptoms cleared promptly with every patient on cessation of therapy.

## COMMENT AND SUMMARY

Experience accumulated in the treatment of 103 patients has demonstrated that sulfamerazine is rapidly absorbed from the gastrointestinal tract and is rather slowly excreted by the kidney. Adequate drug levels can be maintained by doses administered at eight hour intervals. The drug readily diffuses into pleural fluid in concentrations approximating that of the blood and into spinal fluid in concentrations approaching 50 per cent of that in the blood. Patients tolerate sulfamerazine well, side effects being few in number.

Therapeutic results in meningococcic, pneumococcic, streptococcic and colon bacillus infections were satisfactory and compared favorably with those reported for sulfadiazine.

The toxicity of sulfamerazine has been critically evaluated. The incidence of hypersensitivity (drug fever and rashes) seems to be about the same as that observed with other sulfonamide derivatives. Evidence of kidney and urinary tract complications was more frequent than was anticipated from pharmacologic data and preliminary tests in experimental animals.[2] Crystalluria without hematuria was observed in 6.8 per cent of the series. This complication was benign in all instances. One patient without hematuria or crystalluria had concretions of acetylsulfamerazine in both ureters at autopsy. This patient had received large amounts of the drug and his fluid intake was suboptimal. It is probable that the incidence of crystalluria would have been lower if more fluids had been administered or if the urine had been alkalized.

Hematuria was noted in 8.7 per cent of the patients. In consideration of the incidence of hematuria it should be borne in mind that in all but 1 (possibly 2) instances this complication occurred in patients with meningococcic meningitis who received particularly large doses of the drug because of the serious nature of the infection. The occurrence of hematuria could not, however, be related to the blood concentration of the drug. Certain of the patients received a lower fluid intake than was planned. The average fluid intake for the preceding days in 2 of the 3 cases of gross hematuria was only 1,730 and 1,875 cc. respectively. These cases may give some indication of the results to be expected in tropical climates. Since 4 of the 9 patients had hemorrhagic skin manifestations, the suggestion is made that hematuria resulted in certain instances from similar lesions in the kidney. It may be noted further that hematuria was sought for by daily examinations of urinary sediment and that in 6 of the 9 cases the hematuria was discovered only by microscopic examination. It is important to point out also that the hematuria subsided promptly in each case without any evidence of embarrassment to kidney function.

The chief reason for clinical trial of sulfamerazine at this time was the possibility that it might produce fewer and less severe urinary complications than sulfadiazine in warm climates under military conditions. Our experience confirms the previous reports that less of the drug is needed for comparable blood levels, but no conclusion can be drawn as to whether urinary complications occurred more or less often than would have been the case had sulfadiazine been used on the same patients. In certain of these cases circumstances under which the drug was administered were such as to offer an excellent opportunity for urinary complications, and it seems likely that the accumulated results of other observers may indicate that sulfamerazine produces fewer renal complications than sulfathiazole and sulfadiazine.

**Expansion of Intestinal Gas.**—In an ascent to 38,389 feet, one volume of gas originally in the intestinal tract at sea level now occupies 5 volumes. This expansion of gas causes distention and abdominal discomfort in the aviator ascending to such altitudes and may cause respiratory and circulatory distress if the expansion of the gas forces the diaphragm to push up on the heart and lungs.—Gemmill, Chalmers L.: Physiology in Aviation, Springfield, Ill., Charles C Thomas, Publisher, 1943.

# THE CHEMOTHERAPY OF INTRACRANIAL INFECTIONS

## III. THE TREATMENT OF EXPERIMENTAL STAPHYLOCOCCIC MENINGITIS WITH INTRATHECAL ADMINISTRATION OF PENICILLIN

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AND
WILLIAM F. MEACHAM, M.D.
NASHVILLE, TENN.

The great promise of penicillin as an antibacterial agent has recently received wide publicity, even in the lay press. The discovery of its antibacterial activity by Fleming [1] in 1929 and the outstanding investigations of Chain, Florey and their co-workers [2] beginning in 1940 have been reviewed by Hobby, Meyer, Dawson and Chaffee [3] (who also contributed valuable observations of their own). A recent summary of early clinical observations in Great Britain has been published by the Floreys [4] and extensive investigation of the use of penicillin is being carried on in this country.[5]

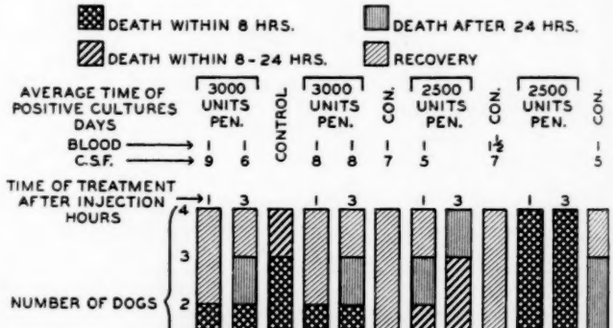


Chart 1.—Effects of a single intravenous injection of penicillin in staphylococcic meningitis.

The experimental study to be reported herein was undertaken as one of a series of investigations of the treatment of infections of the central nervous system and its coverings.[6] This report will be limited to consideration of the effects of penicillin in experimental staphylococcic meningitis.

Read before the Harvey Cushing Society, New York, May 8, 1943.
From the Department of Surgery, Vanderbilt University School of Medicine.
The penicillin was furnished by E. R. Squibb and Sons, New Brunswick, N. J., through the kindness of Dr. George Harrop.
The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Vanderbilt University.

1. Fleming, Alexander: An Antibacterial Action of Cultures of Penicillium, with Special Reference to Their Use in Isolation of B. Influenzae, Brit. J. Exper. Path. **10:** 226 (June) 1929.
2. Chain, E.; Florey, H. W.; Gardner, A. D.; Jennings, M. A.; Orr-Ewing, J.; Sanders, A. F., and Heatley, N. G.: Penicillin as a Chemotherapeutic Agent, Lancet **2:** 226 (Aug. 24) 1940. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, ibid. **2:** 177 (Aug. 16) 1941.
3. Hobby, Gladys L.; Meyer, Karl; Dawson, M. H., and Chaffee, Eleanor: The Antibacterial Action of Penicillin, J. Bact. **43:** 11 (Jan.) 1942.
4. Florey, M. E., and Florey, H. W.: General and Local Administration of Penicillin, Lancet **1:** 387 (March 27) 1943.
5. Penicillin, Statement Released by the Committee on Medical Research, J. A. M. A. **122:** 235 (May 22) 1943.
6. Pilcher, Cobb.; Angelucci, Ralph, and Meacham, W. F.: Convulsions Produced by the Intracranial Implantation of Sulfathiazole, J. A. M. A. **119:** 927 (July 18) 1942. Meacham, W. F.; Angelucci, Ralph; Benz, E., and Pilcher, Cobb.: The Chemotherapy of Intracranial Infections: II. The Clinical and Pathologic Effects of the Intracranial Introduction of Sulfanilamide, Sulfathiazole and Sulfadiazine in Normal Dogs, to be published.

METHODS AND RESULTS

Dogs weighing 7 to 10 Kg. were employed in all experiments. Meningitis was produced by injection of 0.1 cc. of a saline suspension of a strain of hemolytic Staphylococcus aureus into the cisterna magna. This volume contained approximately 400 million organisms. Filtrates of cultures of this organism showed no evidence of toxin formation.

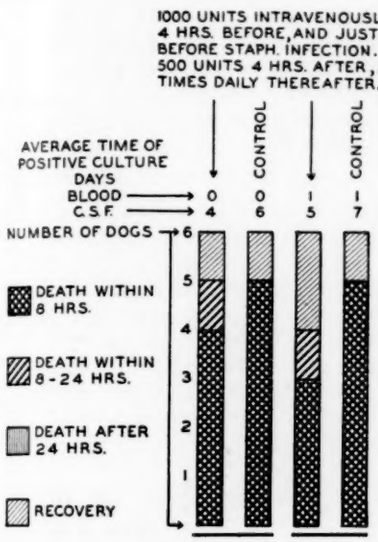
1000 UNITS INTRAVENOUSLY 4 HRS. BEFORE, AND JUST BEFORE STAPH. INFECTION. 500 UNITS 4 HRS. AFTER, 5 TIMES DAILY THEREAFTER.
CONTROL
CONTROL
AVERAGE TIME OF POSITIVE CULTURE DAYS
BLOOD → 0 0 1 1
C.S.F. → 4 6 5 7
NUMBER OF DOGS → 6
DEATH WITHIN 8 HRS.
DEATH WITHIN 8-24 HRS.
DEATH AFTER 24 HRS.
RECOVERY

Chart 2.—Effects of intravenous penicillin therapy in staphylococcic meningitis.

In order to insure that the virulence of the organism should be as nearly constant as possible in successive groups of experiments, the following method of preparation was employed: The organism selected was "passed through" the spinal fluids of a number of dogs until it consistently produced a fulminating fatal meningitis. It was then cultured in a large volume of beef infusion broth containing 10 per cent human plasma for sixteen hours. Finally, small quantities of this culture were sealed in a large number of small glass ampules. The latter were placed in a large container of alcohol, which in turn was kept packed in solidified carbon dioxide in a freezing chamber. The contents of one of these ampules were used for each group of experiments. Each group consisted of 12 dogs. In some groups 6 were treated and 6 served as controls. In others 4 had treatment at one time, 4 at another and 4 served as untreated controls.

Necropsy was performed and microscopic studies were made in most of the experiments, but there were

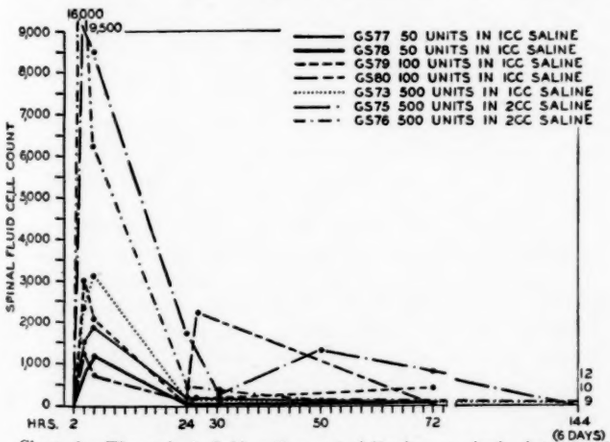
GS77 50 UNITS IN ICC SALINE
GS78 50 UNITS IN ICC SALINE
GS79 100 UNITS IN ICC SALINE
GS80 100 UNITS IN ICC SALINE
GS73 500 UNITS IN ICC SALINE
GS75 500 UNITS IN 2CC SALINE
GS76 500 UNITS IN 2CC SALINE
SPINAL FLUID CELL COUNT
HRS. 2 24 30 50 72 144 (6 DAYS)

Chart 3.—The spinal fluid cell count following a single intrathecal injection of penicillin.

no significant findings other than the varying degrees of meningeal inflammation which would be expected.

For statistical evaluation of results in this type of experiment only two criteria are of real significance, namely mortality rate and duration of life. These two factors are shown in the accompanying charts.

*Intravenous Therapy.*—When the first of these studies was begun the amount of penicillin available was extremely small. For this reason the effects of a single large (2,500-3,000 Florey units) intravenous dose given either one hour or three hours after injection of staphylococci were determined (chart 1). It is sufficient to say of the results that, although there was considerable variation in different groups, no significant beneficial effect of the treatment was observed.

When more penicillin became available,[7] an additional series of experiments was carried out in which intravenous therapy was begun before injection of staphylococci and continued in equally spaced doses of 500 units five times daily, as shown in chart 2. Of the 24 dogs, 3 treated and 2 control animals recovered. Seven treated animals, as compared with 10 controls, failed to survive eight hours.

*Intrathecal Therapy.*—When these experiments were begun there was no published report of the intrathecal injection of penicillin. Since intravenous treatment of staphylococcic meningitis had not proved effective, it seemed advisable to determine the value of intrathecal therapy. First, however, the effects of intracisternal injections of penicillin in normal dogs were studied.

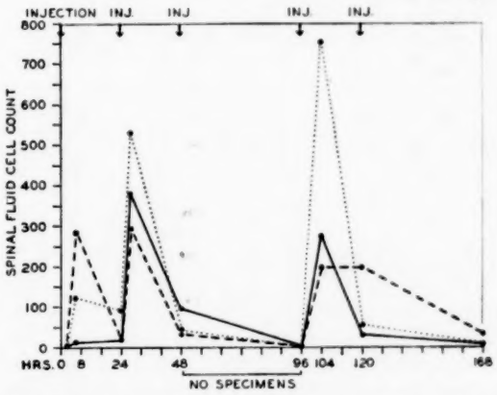


Chart 4.—The spinal fluid cell count on normal dogs following repeated injections of 50 units of penicillin.

Such injections produced transitory meningeal reactions whose intensity was roughly proportional to the dose (chart 3). Repeated doses at twenty-four hour intervals increased the severity of the reactions only slightly (chart 4). No significant neurologic or systemic phenomena were observed. The animals were alert, took food and fluids normally and had no significant febrile reactions.

On the basis of these observations it was decided to use an intrathecal dosage of 50 Florey units administered once daily.[8] Treatment was begun either one hour before or one hour after injection of staphylococci (chart 5).

In every one of the four series the mortality rate was much lower and the number of animals which either recovered or lived more than twenty-four hours was far higher in the treated than in the control groups.

In the forty-seven experiments only 1 of 15 control dogs (6⅔ per cent) recovered, whereas thirteen of the 32 treated animals (46.3 per cent) recovered (chart 6).

The number of animals which recovered was greater in the groups in which treatment was begun after injec-

7. Through the auspices of the Committee on Medical Research of the Office of Scientific Research and Development.

8. Later observations, to be published elsewhere, have shown that much larger and more frequent intrathecal doses are well tolerated and we regret that they were not employed in these experiments.

tion of staphylococci than in those in which treatment was begun before injection.

It is significant that the cerebrospinal fluid cultures remained positive for several (or many) days even in those treated animals which recovered. This is in support of the now generally accepted concept of penicillin as a bacteriostatic agent.

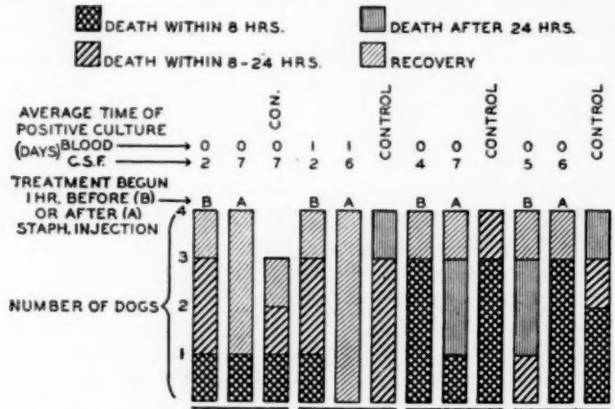


Chart 5.—The effect of treatment of staphylococcic meningitis with daily intracisternal injections of 50 units of penicillin.

At no time were any harmful effects attributable to penicillin observed.

## COMMENT

A survey of all our experiments (chart 6) suggests that frequent intravenous medication with penicillin may be of slight benefit in staphylococcic meningitis. Such benefit, if actually present at all, was very limited in this study. This is not surprising in view of the recent observation of Rammelkamp and Keefer [9] that "penicillin does not pass through the blood-brain barrier in significant quantities following an intravenous injection of the substance."

On the other hand, our experiments indicate clearly that intrathecal administration of penicillin (even in widely spaced doses now known to be too small) may greatly reduce the mortality rate.

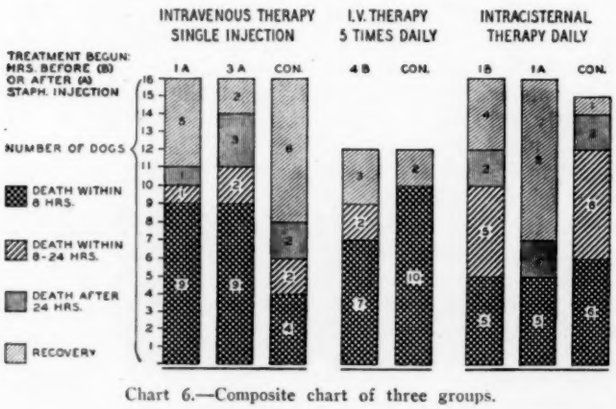


Chart 6.—Composite chart of three groups.

Since these experiments were completed, Rammelkamp and Keefer [10] have reported studies on the effects of intrathecal injection of single large doses of penicillin in normal human beings as well as in several subjects with various diseases of the central nervous system. Their observations indicate that penicillin is absorbed slowly from the cerebrospinal fluid (although more rapidly in the presence of meningitis than in normal subjects). They also demonstrated the same meningeal reaction which was observed in our experiments. The only toxic reactions observed by them were vomiting and headache in one subject (after intrathecal injection of 10,000 Florey units).

From our experiments it seems justifiable to conclude that intrathecal injection of penicillin is a safe form of therapy and to suggest that this method of treatment will probably be of great value in clinical cases of staphylococcic meningitis.


## SUMMARY

Intravenous treatment of experimental staphylococcic meningitis was found to have little if any beneficial effect.

Penicillin, when injected intrathecally, even in relatively large doses, produced a pleiocytosis in the cerebrospinal fluid but no other significant toxic effect.

Intrathecal treatment of experimental staphylococcic meningitis with relatively small doses of penicillin greatly reduced the mortality rate (from 93 per cent in control experiments to 54 per cent in treated animals).

It is suggested that intrathecal penicillin therapy will probably be valuable in treatment of clinical staphylococcic meningitis.


9. Rammelkamp, C. H., and Keefer, C. S.: J. Clin. Investigation, to be published; cited by Rammelkamp and Keefer.[10]

10. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Toxicity of Penicillin Administered by Intrathrecal Injection, Am. J. M. Sc. **205**: 342 (March) 1943.

# THE PROBLEM OF THE ETIOLOGY OF RAT BITE FEVER

### REPORT OF TWO CASES DUE TO SPIRILLUM MINUS


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Evidence at present indicates that two different infectious agents may produce the disease known as rat bite fever: Spirillum minus and Streptobacillus moniliformis. The clinical manifestations of these two infections may be so similar that differentiation is possible only by demonstration of the causative organisms.[1] Recent reviews of the literature on rat bite fever in America show that approximately 150 cases have been reported and that the majority were regarded as Spirillum minus infections, although actual demonstration of the parasite by animal inoculation was carried out in only 23 of the cases.[2] Dawson and Hobby have questioned this evidence because the laboratory animals used in making the diagnosis may be naturally infected with spirilliform organisms and because Spirillum minus has not been demonstrated in the blood of persons suffering from rat bite fever.[3] Nevertheless it must be accepted that Spirillum minus can produce a disease in man typical of rat bite fever, since a number of patients with neurosyphilis have been inoculated with Spirillum minus for therapeutic purposes and the typical clinical picture of rat bite fever has resulted.[4] Brown


Dr. R. S. Leadingham gave technical assistance in identifying Spirillum minus.

From the Medical Service of Grady Hospital and the Department of Medicine, Emory University School of Medicine.


1. Brown, T. M., and Nunemaker, J. C.: Bull. Johns Hopkins Hosp. **70**: 201 (March) 1942.

2. Larson, C. L.: Pub. Health Rep. **56**: 1961 (Oct. 3) 1941. Packchanian, A., and Sweet, L. K.: Med. Ann. District of Columbia **10**: 95 (March) 1941. Rogliano, A. G.: Surgery **11**: 632 (April) 1942. Brown and Nunemaker.[1]

3. Dawson, M. H., and Hobby, G. L.: Tr. A. Am. Physicians **54**: 329, 1939.

4. Solomon, H. C.; Berk, Arthur; Theiler, Max, and Clay, C. L.: The Use of Sodoku in the Treatment of General Paralysis, Arch. Int. Med. **38**: 391 (Sept.) 1926. Hershfield, A. S.; Kibler, O. A.; Colby, Selma; Koenig, M. T.; Schmid, O. W., and Saunders, Anny M.: Sodoku Treatment in Paresis, J. A. M. A. **92**: 772 (March 9) 1929.

and Nunemaker, after studying the available evidence, expressed the opinion that infection with either of the two organisms may follow rat bite but thought that Streptobacillus moniliformis infection is probably the commoner of the two. The reasons for uncertainty are that only in a few cases has search for both organisms been made and that the laboratory procedures used have not always been reliable. In the present article I report two additional cases of rat bite fever. Spirillum minus was isolated in both instances, and cultures for Streptobacillus moniliformis were negative. Certain technical details of the laboratory procedures are considered.

## REPORT OF CASES

CASE 1.—*History.*—L. G. H., a white boy aged 2 years, was bitten by a rat on the thumb and first finger of the right hand while asleep on Dec. 12, 1942. He was brought immediately to the emergency clinic of Grady Hospital, where the wound, described as "multiple lacerations," was cleaned and dressed with 1 per cent sulfathiazole ointment. Antitetanus serum was administered. The wound healed promptly and the child remained well until Jan. 18, 1943, thirty-seven days later, when his mother noted that his skin was hot, that he was listless and that there were several small red spots on his face and arms. The next day he improved rapidly and the rash disappeared. Four days later he again became listless and feverish and was brought to the hospital. Examination showed a normally developed child, who appeared acutely ill. The temperature was 104 F. His skin was hot and dry, and several large, irregular, erythematous areas were present on his face, neck, abdomen and right arm. There were some swelling and induration at the site of the rat bite. The right axillary nodes were palpable. There were no other physical findings. The erythrocyte count was 3,150,000 per cubic millimeter, hemoglobin was 8.1 Gm. per hundred cubic centimeters and leukocytes numbered 6,500 per cubic millimeter with 72 per cent polymorphonuclears. The urine was normal. Agglutination tests with typhoid, proteus OX19 and brucella were negative. The blood Kahn reaction on admission was "doubtful," two days later it was 2 plus and three days later it was "doubtful." No further Kahn tests were done. The tuberculin test was negative.

*Course.*—The patient's temperature variations and the significant laboratory studies are shown graphically in chart 1. It will be observed that he had three febrile episodes, separated by periods of two to three days of normal temperature. During each of the febrile periods a blotchy erythematous rash was noted on his face and extremities. Between the sixteenth and

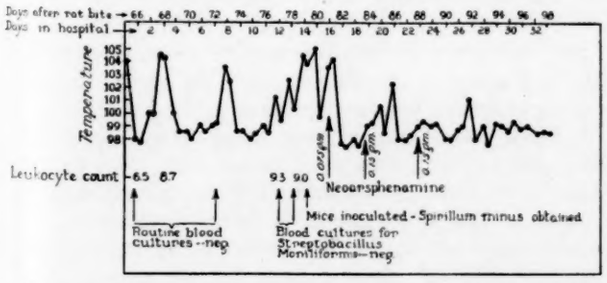


Chart 1.—Course of temperature in case 1, together with significant laboratory and therapeutic procedures.

twenty-third hospital days three intravenous injections of neoarsphenamine were given. Following these he had one brief rise of temperature but thereafter remained afebrile and was apparently quite well when discharged from the hospital on the thirty-third day. He was seen again at a follow-up visit two months later and was still free from symptoms.

*Special Laboratory Examinations.*—Routine blood cultures in tryptose phosphate broth on the first and eighth hospital days gave no growth. On the thirteenth and fourteenth hospital days blood cultures were made according to the technic recommended by Brown and Nunemaker for Streptobacillus moniliformis with 20 per cent fresh rabbit serum in tryptose phosphate broth. Again there was no growth. In an attempt to demonstrate the presence of Spirillum minus 4 mice were inoculated with the patient's blood. Each received 0.25 cc. of fresh uncitrated blood intraperitoneally. The blood of each mouse was examined by dark field microscope before inocula-

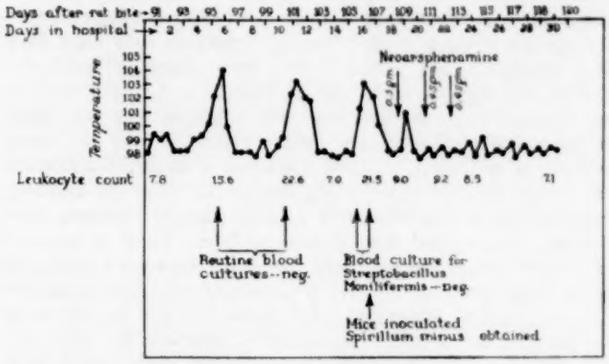


Chart 2.—Course of temperature in case 2, together with significant laboratory and therapeutic procedures.

tion and also on the seventh and fourteenth days afterward, but no spirilla were found. On the sixteenth day, however, Spirillum minus was observed in the blood of 1 of the 4 mice, and on the eighteenth day it was present in the blood of all 4 mice. During the succeeding four weeks Spirillum minus was easily demonstrated in the blood of all 4 mice.

CASE 2.—M. L. H., a white woman aged 59, married, came to the emergency clinic of Grady Hospital on the night of Nov. 2, 1942 a few hours after she had been bitten by a rat while sleeping. There was a small puncture wound on the right side of her face near the angle of the jaw. This was treated with chromic acid, and she was given antitetanus serum. On November 19, seventeen days later, she returned to the clinic because of a soft swelling in the region of the bite. Her temperature was 99.6 F. The swelling seemed fluctuant and was incised, but no pus was obtained. She returned for a dressing on November 23, at which time the wound was almost healed. She was not seen again until Feb. 1, 1943, when she returned to the medical clinic complaining of pains in her extremities, weakness, loss of appetite, spells of nausea and vomiting, and some loss of weight. She did not remember dates very accurately, but questioning indicated that she had felt well until about December 25, which was fifty-three days after the rat bite. At that time she had a febrile illness which she thought was "influenza." This had been characterized by chilly sensations, fever, aching in the muscles and a "head cold" and had lasted for approximately two weeks. From that time until admission to the hospital she was never entirely well. There had been episodes every few days of feverishness, chilliness, nausea and vomiting. About January 10 she had noted a painful swelling of her hands, forearms and elbows, and one week later there was a similar swelling of her feet and ankles, first on the left side and then on the right. She was admitted to the hospital for study. On physical examination she appeared poorly nourished but not acutely ill. There was no fever. The skin was somewhat dry and scaly. A few small, nontender lymph nodes were noted in the right submaxillary and posterior cervical regions. The heart and lungs were normal. The blood pressure was not elevated. The abdomen was not tender; the liver edge was just palpable; the spleen was not felt. Over the right foot and leg was a soft pitting edema, and this entire area was somewhat tender on pressure. Dorsiflexion of the right foot was painful. These findings were interpreted as evidence of thrombophlebitis in the right leg. Routine laboratory examina-

tions showed erythrocytes 3,600,000 per cubic millimeter, hemoglobin 9.5 Gm. per hundred cubic centimeters, leukocyte count 7,800 with 87 per cent polymorphonuclears; sedimentation rate 82 mm. per hour; blood Kahn test negative; urine normal.

*Course.*—The patient's temperature and significant laboratory studies during her hospital stay are shown graphically in chart 2. It will be noted that she had three febrile episodes at approximately five day intervals and that no further episodes occurred after she was given injections of neoarsphenamine. The leukocyte count rose sharply when she developed fever. A diagnosis of rat bite fever was not suspected until some days after admission, and initial studies were concerned with the function of her stomach and gallbladder. On the twelfth hospital day, when she had fever, the following note was made on her record: "There is a diffuse erythema over the outer surfaces of the arms, a slight splotchiness over the abdomen, and the skin of the right leg below the knee is diffusely reddened and warm. There is a fairly marked erythema surrounding the original area of the rat bite. There is no new lymphadenopathy, though there are small nontender nodes in the submaxillary region." At the onset of the third paroxysm of fever, special laboratory procedures for the identification of Spirillum minus and Streptobacillus moniliformis were carried out, and following that she was given three intravenous injections of neoarsphenamine at two day intervals, as indicated in the chart. This effected a pronounced and rapid clinical improvement; the nausea and vomiting ceased and the pain and swelling in her extremities disappeared. She left the hospital, feeling entirely well, on the thirty-first day. Four weeks later she returned to the outpatient clinic for follow-up and reported herself entirely well.

*Special Laboratory Examinations.*—Routine blood cultures on the sixth and eleventh hospital days were negative. On the sixteenth and seventeenth days two more cultures were made according to the technic of Brown and Nunemaker, using 20 per cent fresh rabbit serum in tryptose phosphate broth, but Streptobacillus moniliformis was not obtained. In an attempt to find Spirillum minus, mice were inoculated with the patient's blood on the seventeenth day. Four mice each received 0.5 cc. of fresh uncitrated blood intraperitoneally. One of these mice was killed by its cage mate two days later. Examinations of the blood of the remaining 3 mice were made on the third, twelfth and fourteenth days after inoculation, and Spirillum minus was not found. On the seventeenth day Spirillum minus was found in the blood of 1 of the mice but not in the other 2. On the twenty-first and thirtieth days the same mouse was positive and there appeared to be a considerably larger number of spirilla present. The organisms were never found in the blood of the other 2 mice.

## LABORATORY EXAMINATIONS IN RAT BITE FEVER

Streptobacillus moniliformis has been isolated by routine blood culture on a number of occasions, but Brown and Nunemaker advise a modification of the routine procedure when this organism is suspected.[1] Their technic consists essentially in centrifuging citrated blood and then culturing the blood cell residue in test tubes containing fresh serum and a nutrient broth. Under these conditions the "fluff ball" colonies are easily seen and can be withdrawn with a pipet for staining or subculture. Wayson's stain was recommended for studying the morphology of the organisms. This technic was carefully followed in the present cases. Any formation on the surface of the blood cell layer which was suspected of containing bacteria was stained by Wayson's and other methods, but the results were always negative.

Suitable precautions were taken to eliminate the possibility of preinfection in the mice used in the isolation of Spirillum minus from these 2 patients. Not only were there several negative preliminary examinations on the test mice but as a further precaution 14 cage mates which had not been inoculated were also examined. Spirillum minus was not present in the blood of any of the animals. Furthermore, the animals used in the 2 cases were different breeds of mice. Those used in case 1 were brown mice which had been obtained from South Carolina, while those used in case 2 were white mice which had been obtained in Atlanta.

Spirillum minus is not difficult to identify when present in the peripheral blood of a mouse. A drop of blood, obtained by snipping off the end of the tail with scissors, is pressed out very thinly with a cover slip on a slide, and the preparation is examined in a dark field microscope. McDermott has written an extensive description of this organism.[5] The most striking characteristic is its extremely rapid motility. In a fresh preparation it darts in and out of the field very rapidly; however, after an hour or more the motility is often considerably slower. Under these circumstances it is easier to observe the morphology. The organisms are 2 to 5 microns in length, and there are usually two to five spirals. Flagella can be seen as a hazy appearance at the ends. In addition to visibility in the dark field they can also be seen in stained preparations. Ripley and Van Sant have published excellent photomicrographs.[6]

Emphasis is needed on the point that the appearance of the spirillum in the peripheral blood of an inoculated animal may not occur until the third week. Some textbooks and writings on the subject state that it appears between the fifth and fourteenth days. In the 2 cases reported here the spirillum was not found until the sixteenth and seventeenth days, and in other instances the first appearance has been as late as the thirty-seventh day.[5]

## COMMENT

These 2 patients with rat bite fever were in the hospital at the same time but were otherwise not related. Some of the clinical features showed striking similarities. The incubation periods were long, the skin eruptions resembled each other closely, the fevers were of the same type, and both infections responded promptly to neoarsphenamine therapy. Points of dissimilarity were the prominence of nausea and vomiting in case 2 and the leukocytosis which accompanied the febrile periods in case 2. Neither patient exhibited evidence of arthritis while under observation, although patient 2 gave a history of swelling around the wrists, elbows, knees and ankles before admission to the hospital.

It is of interest that three other cases of rat bite fever due to Spirillum minus have been identified in Atlanta,[7] whereas in Brown and Nunemaker's study of 8 cases in the Baltimore area Streptobacillus moniliformis appeared to be the etiologic agent in every instance. Possibly these differences are due to variations in the parasites harbored by rats in different localities.

## SUMMARY

In 2 cases of rat bite fever Spirillum minus was isolated from the blood by mouse inoculation. Cultures of the blood for Streptobacillus moniliformis were negative.

5. McDermott, E. N.: Quart. J. Med. **21**: 433 (April) 1928.
6. Ripley, H. S., and Van Sant, Helen M.: Rat Bite Fever Acquired from a Dog, J. A. M. A. **102**: 1917 (June 9) 1934.
7. Leadingham, R. S.: Am. J. Clin. Path. **8**: 333 (May) 1938.

# THE PROPHYLACTIC VALUE OF SULFADIAZINE

## IN THE CONTROL OF MENINGOCOCCIC MENINGITIS

COLONEL DWIGHT M. KUHNS
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CAPTAIN CARL T. NELSON
MEDICAL CORPS, ARMY OF THE UNITED STATES

CAPTAIN HARRY A. FELDMAN
MEDICAL CORPS, ARMY OF THE UNITED STATES

AND

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From Jan. 1, 1943 to April 30, 1943 more than 1,300 cases of meningococcic meningitis occurred among military personnel in the Fourth Service Command. During this period the attack rate for the disease varied widely from post to post. In some installations only sporadic cases were found; in others the number of cases reached epidemic proportions. Generally speaking, however, the disease was more prevalent in stations where large numbers of recently inducted men were assembled for training purposes.

The customary control measures employed during outbreaks of meningococcic meningitis include quarantine, prevention of overcrowding, protection from fatigue and exposure, and the prompt hospitalization or isolation of all cases of common respiratory illnesses. It is admitted, however, that these measures are only partially effective and, under conditions of active military training, can be properly applied only with considerable difficulty. It seemed desirable, therefore, to seek additional means of controlling this disease, particularly among the relatively "unseasoned" recent inductees.

To be useful under military conditions, any control measure proposed must be applicable to large numbers of individuals without causing serious interruptions in daily activities. The remarkable effectiveness of sulfadiazine in the treatment of meningococcic meningitis suggested that it might be of prophylactic value in the control of this disease among troops. There is evidence that other sulfonamides, namely sulfanilamide and sulfapyridine, may have some prophylactic value in curbing outbreaks of meningitis and eliminating meningococci from the nasopharyngeal mucosa.[1] Dingle and his associates[2] have pointed out that meningococci disappear promptly from the nasopharynx of patients undergoing treatment with sulfadiazine. This implies that sulfadiazine may be effective in the treatment of meningococcus carriers. Although the exact role of the carrier in relation to the spread of meningococcic meningitis is not entirely clear, it seems logical that a measure which can quickly reduce the carrier rate to a low level may be valuable in retarding sharp outbreaks of this disease. Indeed, reports transmitted from the Office of the Surgeon General have indicated that sulfadiazine has been of value in controlling meningitis at several army posts in recent months.

Studies undertaken at the Fourth Service Command Laboratory have shown that meningococci are rapidly eliminated from the nasopharynx following the peroral administration of 3 Gm. of sulfadiazine daily for three days. In a small series of persistent carriers treated in this manner, nasopharyngeal cultures became negative for meningococci twenty-four hours after the initiation of therapy, and repeated nasopharyngeal cultures, obtained at weekly intervals, remained negative for varying periods of observation up to eight weeks. These results suggested that it might be possible, by treating all members of a closed group with sulfadiazine at one time, to decrease the number of individuals harboring meningococci during epidemic periods to a point where few, if any, cases of meningitis would occur. Our purpose in this communication is to report the results of the large scale prophylactic administration of sulfadiazine to more than 15,000 soldiers stationed at two posts where meningococcic meningitis was particularly prevalent during the spring of 1943.

### CAMP A

*Occurrence of Meningococcic Meningitis.*—Camp A is a newly constructed installation located in rural Mississippi. The camp was first occupied by troops in August 1942, but as late as January 1943 the total military population had reached only 3,100. Thereafter the strength of the post rose rapidly until on March 15, 1943 over 34,000 soldiers were stationed there. These included approximately 15,000 men who had arrived at Camp A during the latter part of February 1943 to form the M Infantry Division. The majority of this division was made up of men under 20 years of age who had been inducted into service during the preceding sixty days and who had been assembled from all regions of the United States. The M Division was barracked in areas III, IV and VI of Camp A (fig. 1). These areas are geographically and functionally separate from one another and at the time of this study were reserved solely for this organization. Two infantry regiments were assigned to area III, while areas IV and VI were occupied by an infantry regiment, the division artillery and special troops. Members of the division were housed in 32 man barracks of the theater of operations type. Forty-two men occupied double decked bunks in each barracks, sleeping in head to foot arrangement. Shortly after arrival at Camp A, all men assigned to the M Division began a course of basic training. The program did not seem to be excessively rigorous, and physical exhaustion was no greater than might be expected in fresh troops recently inducted from civilian life.

From the Fourth Service Command Medical Laboratory, Fort McPherson, Georgia.

The cooperation of Col. S. W. French, M. C., Col. C. G. Souder, M. C., Col. H. M. Thomas Jr., M. C., Col. D. C. Campbell, M. C., Col. T. E. Scott, M. C., Lieut. Col. George Prazak, M. C., Lieut. Col. T. C. Rich, M. C., Major W. B. Malcolm, M. C., Capt. V. D. Francis, M. C., Capt. R. J. Reedy, Sn. C., Capt. S. C. Selkovits, M. C., Capt. M. A. Fath, M. C., Lieut. L. L. Lieberman, M. A. C., Lieut. Saul Freedman, M. A. C., Lieut. M. W. O'Neil Jr., M. A. C., and Lieut. J. R. Klett, M. A. C., greatly facilitated the course of these studies. Miss A. M. Gunderson, Miss P. L. Moorman, Miss L. L. Laffitte, Miss M. E. Askew and Sgt. R. J. Reiber rendered technical assistance.

Appreciation is further expressed to Brig. Gen. J. S. Simmons and Col. Stanhope Bayne-Jones, Preventive Medicine Section, Office of the Surgeon General, U. S. Army, Washington, D. C., for their assistance.

1. Bryant, Joseph, and Fairman, H. D.: Chemotherapy of Cerebrospinal Fever in the Field, Lancet **1:** 923-926 (April 22) 1939. Meehan, J. F., and Merrillees, C. R.: Outbreak of Cerebrospinal Meningitis in Foundling Hospital: Treatment of Carriers with "M. & B. 693," M. J. Australia **2:** 84-90 (July 27) 1940. Seid, S. E.: Meningitis Epidemic Among Navajo Indians, J. A. M. A. **115:** 923-924 (Sept. 14) 1940. Fairbrother, R. W.: Cerebrospinal Meningitis: Use of Sulfonamide Derivatives in Prophylaxis, Brit. M. J. **2:** 859-862 (Dec. 21) 1940. Delafield, M. E.; Straker, Edith, and Topley, W. W. C.: Antiseptic Snuffs, Brit. M. J. **1:** 145-150 (Feb. 1) 1941. Gray, F. C., and Gear, J.: Sulfapyridine M. & B. 693 as a Prophylactic Against Cerebrospinal Meningitis, South African M. J. **15:** 139-140 (April 12) 1941. Awe, C. D.; Babione, R. W., and DeLamater, J. N.: Meningococcic Meningitis in the San Diego Area During 1942, U. S. Nav. M. Bull. **41:** 625-634 (May) 1943.

2. Dingle, J. H.; Thomas, Lewis, and Morton, A. R.: Treatment of Meningococcic Meningitis with Sulfadiazine, J. A. M. A. **116:** 2666-2668 (June 14) 1941.

During the five week period immediately following activation (i. e. from Feb. 15 to March 22, 1943) the weekly hospital admission rate for common respiratory diseases in the M Division rose sharply from 13.5 to 42.9 per thousand. Although all sections of the division contributed to this high incidence of respiratory illnesses, the units of the division housed in areas IV and VI consistently showed a slightly higher attack rate than did the two infantry regiments stationed in area III. During this same length of time the weekly hospital admission rate for common respiratory diseases in all organizations at Camp A other than the M Division fell steadily from 15.9 to 6.2 per thousand.

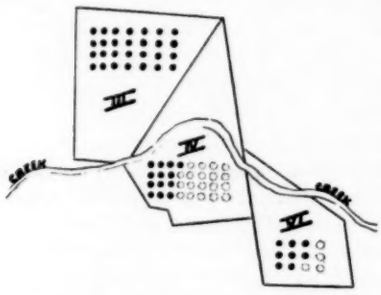


Fig. 1. — Distribution of meningococcic meningitis, M Division, Camp A, 1943. Solid dots, cases from February 21 to March 22. Hollow dots, cases from March 22 to May 16.

The first cases of meningococcic meningitis at Camp A occurred during the week of January 24. During the next eight weeks there were 79 cases of cerebrospinal fever in the camp. Meningitis first appeared in the M Division on February 26. The earliest cases occurred among troops stationed in area III, and it was not until one week later that additional cases were found in the remainder of the division. The first case of meningitis in the M Division was in a man who had arrived at Camp A nine days previously. In all other early cases the time interval between arrival at Camp A and the onset of symptoms exceeded nine days. It is assumed, therefore, that this outbreak of meningitis in the M Division probably developed in situ at Camp A and that no clinically recognizable cases were introduced from other military installations. Of the 79 cases of meningococcic meningitis admitted to the Station Hospital during the period from January 24 to March 21, 49 originated in the M Division. Twenty-eight of these occurred among the troops housed in area III and 21 in the other units of the division. The distribution of these cases, by areas, is shown in figure 1.

To summarize, then, the M Division constituted a large group of men, essentially homogeneous in age and duration of service, who were living under similar environmental circumstances. In the presence of a high incidence of meningococcic meningitis this organization seemed to offer an outstanding opportunity to study, under extraordinarily well controlled conditions, the prophylactic value of sulfadiazine in the control of this disease.

*Method of Study.*—The entire personnel of the organizations quartered in area III were selected for treatment (fig. 1). This group numbered approximately 8,000 men. The remainder of the M Division, namely the 9,300 men barracked in areas IV and VI, served as an untreated control (fig. 1). At the time of institution of prophylactic treatment the weekly attack rate for meningococcic meningitis in both the treated and control groups was slightly greater than 1.3 per thousand.

Before administration of the drug the meningococcus carrier rates in the treated and control groups were estimated. Nasopharyngeal cultures were obtained from 100 individuals selected at random in each group. Sterile bent wire swabs were used to procure material for culture. These were streaked on chocolate agar plates prepared from Bacto-Proteose No. 3 agar and Bacto-Hemoglobin. P-aminobenzoic acid was added to this medium in a concentration of 5 mg. per hundred cubic centimeters. The plates were incubated under reduced oxygen tension in a candle jar for twenty hours at 37 C. Subcultures were then made on the same medium. Identification of meningococci was confirmed by inoculation of differential sugar mediums and macroscopic slide agglutination reactions with polyvalent antimeningococcus horse serum and group specific antimeningococcus rabbit serums. The carrier rate among the troops to be treated was 36.0 per cent; in the control group the rate was 38.0 per cent. The predominant meningococcus found in each instance was group I.

On March 22-24 all individuals in the group to be treated were simultaneously given 1 Gm. of sulfadiazine by mouth three times daily. Thus each man received 9 Gm. of medication. The drug was issued by the officer in command of each unit at the mess hall as the men entered for their meals. A noncommissioned officer ascertained that the troops actually swallowed the tablets. Instructions were issued to the effect that any man who became ill after taking the drug was to report immediately to the dispensary for observation by a medical officer. Each man was also advised to drink at least 1,500 cc. of water daily during treatment.

*Results.*—During an eight week period of observation subsequent to the completion of prophylactic therapy no cases of meningococcic meningitis developed among the 8,000 treated men in area III. At the same time, although the attack rate for the disease exhibited a definite decrease, 23 cases were found among the 9,300 untreated controls. The occurrence of meningococcic meningitis in the treated and control groups, as well as in all organizations at Camp A other than the M Division, from January 24 to May 16, is shown in figure 2. These results clearly suggest that the administration of sulfadiazine to all personnel within a large group at one time may result in the abrupt cessation of an outbreak of meningococcic meningitis.

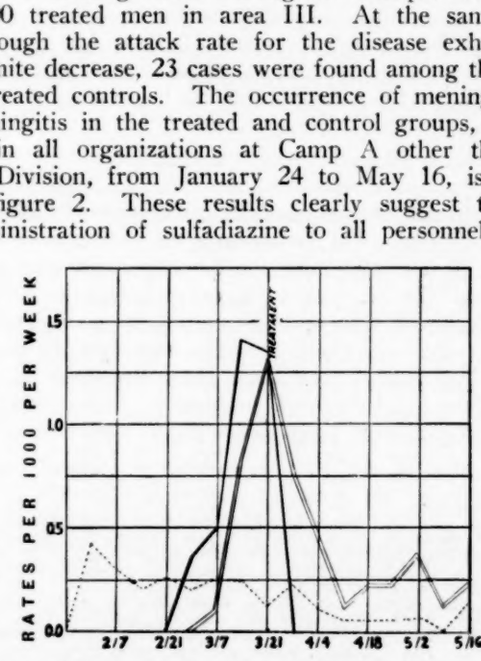


Fig. 2.—Incidence of meningococcic meningitis in treated and control groups and in all organizations other than M Division, Camp A, Jan. 24, 1943 to May 16, 1943. Solid line, treated group. Broken line, all organizations except M Division. Double line, control group.

Additional meningococcus carrier surveys were carried out at intervals in the treated and control groups after the completion of prophylaxis. In each instance nasopharyngeal cultures were obtained from the same individuals employed in the original surveys. The

results of these studies are shown in table 1. These data indicate that the administration of sulfadiazine by mouth effectively lowered the meningococcus carrier rate in the treated group at a time when the incidence of carriers among the untreated controls increased appreciably. It is also interesting that the increase in the carrier rate in the latter group occurred contemporaneously with a decline in the attack rate for meningococcic meningitis among these men.

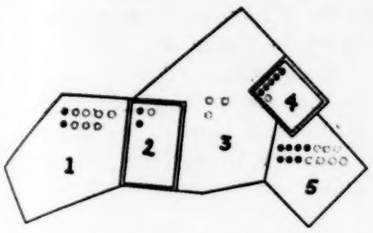


Fig. 3. — Distribution of meningococcic meningitis, N Division, Fort B, 1943. Solid dots, cases from March 21 to April 7. Hollow dots, cases from April 7 to June 2.

During the prophylactic administration of the drug at Camp A, no toxic reactions requiring hospitalization occurred nor was there any interference with the scheduled basic training program of the treated troops. The minimal toxic symptoms frequently noted during sulfadiazine therapy, however, were observed by almost 10 per cent of the men questioned. These included headache, dizziness, loss of visual depth perception, lassitude, tinnitus and nausea. In 2 cases treatment was discontinued because of the development of generalized skin eruptions. Blood sulfadiazine levels, obtained from samples of 10 men on duty subsequent to this study, showed average fasting levels, following each day of treatment for three days, of 5.1, 5.1 and 4.5 mg. per hundred cubic centimeters respectively. The method of Bratton and Marshall [3] was used.

### FORT B

*Occurrence of Meningococcic Meningitis.*—Fort B is a large, permanent military reservation with facilities for housing more than 50,000 men. This post has had a large military population for the past two years, but the majority of the troops now in residence have been there less than twelve months.

The N Division is a relatively new organization which arrived at Fort B in the latter part of March 1943. Most of the troops were young inductees who had been in service less than sixty days. These men had been assembled from widely scattered parts of the United States in a manner similar to that already described for the M Division at Camp A.

The section of Fort B occupied by the N Division is shown in figure 3. Areas 2 and 4 were each occupied by an infantry regiment, while the remainder of the division was assigned to areas 1, 3 and 5. The men were housed in two story, 63 man barracks and slept in cots arranged in head to foot fashion. Shortly after arrival a course of basic training was instituted for all members of the division. This program was comparable to that prescribed for the M Division at Camp A.

During the four weeks immediately following the arrival of the N Division at Fort B, i. e. from March 14 to April 10, the weekly hospital admission rate for common respiratory diseases in the division rose from 7.0 to 24.2 per thousand. This was in contrast to the decline in weekly admission rates for common respiratory illnesses from 9.0 to 4.7 per thousand which occurred in all organizations other than the N Division at Fort B during the same period. The sharp rise in the incidence of upper respiratory illnesses in the N Division immediately after its activation was strikingly similar to the rise previously observed among the newly assembled troops of the M Division at Camp A shortly after their arrival.

From Nov. 13, 1942 to April 6, 1943, 147 cases of meningococcic meningitis were admitted to the Station Hospital at Fort B. One hundred and twenty-four of these occurred during the period from Jan. 1, 1943 to March 31, 1943. During the latter half of February and the first three weeks of March, however, the incidence of cerebrospinal fever at this post fell slowly until only sporadic cases were found. Only after the arrival of the N Division did the incidence of the disease again show an increase. Meningitis first appeared in the N Division during the week of March 21. The earliest cases occurred among troops in divisional areas 1 and 5 (fig. 3). It was not until the first week of April that cases of the disease were found among the members of the infantry regiments stationed in areas 2 and 4. From March 21 to April 6, 16 cases of meningococcic meningitis appeared in the N Division. The distribution of these cases within the divisional area is shown in figure 3. In 3 instances the disease developed in men who had arrived at Fort B less than ten days previously. It is possible, therefore, that these men were in the incubation period of the disease when they were introduced into the population of the N Division.

The conditions observed in the N Division were similar in virtually all important respects to those previously encountered in the M Division at Camp A. Thus the N Division seemed to present another opportunity to study, under well controlled circumstances, the possible prophylactic value of sulfadiazine in checking epidemics of meningococcic meningitis among large groups of individuals.

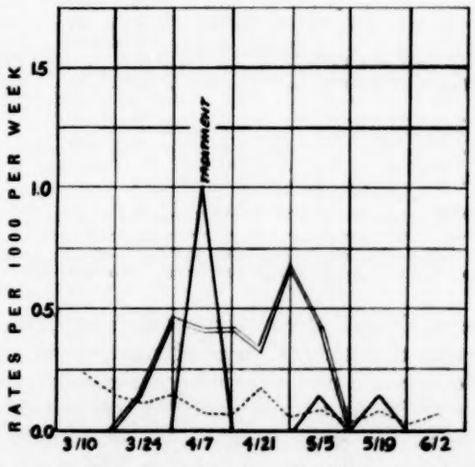


Fig. 4.—Incidence of meningoccic meningitis in treated and control groups and in all organizations other than N Division, Fort B, March 10, 1943 to June 2, 1943. Solid line, treated group. Broken line, all organizations except N Division. Double line, control group.

*Method of Study.*—Largely because of the sharp rise in the incidence of meningitis which had been observed among the troops living in areas 2 and 4, these men were selected for prophylactic therapy (fig. 3). The total strength of the group to be treated was approximately 7,000. The remainder of the N Division, which included all organizations quartered in areas 1, 3 and 5,

3. Bratton, A. C., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128:** 537-550 (May) 1939.

served as a control. The approximate strength of this group was 9,500 men. During the week immediately prior to therapy, the weekly attack rate for meningococcic meningitis in the group to be treated had risen rapidly from 0.0 to 1.0 per thousand. This compared with a weekly rate of 0.41 per thousand in the control group at that time.

Before the institution of prophylactic therapy the incidence of meningococcus carriers in the treated and control groups was estimated in a manner similar to that previously employed at Camp A. The carrier rate in the group to be treated was 30.0 per cent; in the control group the rate was 29.0 per cent. Of the meningococci found in these carriers, 37.2 per cent were group I micro-organisms.

*Results.*—In a period of observation which extended for eight weeks after the institution of treatment, 2 cases of meningococcic meningitis occurred in the N Division among troops who received the drug.[4] In the untreated group, however, 17 cases were found during this time. These results are shown graphically in figure 4. For purposes of comparison the hospital admission rate for meningococcic meningitis in all organizations other than the N Division from March 10 to June 2 is also included in figure 4. These data confirm the findings initially observed at Camp A and in addition indicate that the prophylactic peroral administration of as little as 2 Gm. of sulfadiazine daily for two days is effective in curbing outbreaks of cerebrospinal fever among large numbers of troops.

TABLE 1.—*Incidence of Meningococcus Carriers in Treated and Control Groups*

Camp A, March 20-May 31, 1943

| | Treated Group | | | | | | | Control Group | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Meningococcus Grouping | | | | | | | Meningococcus Grouping | | | |
| Date of Culture | Number Cultured | Number Positive | Per Cent Positive | I | II | IIa | Polyvalent* | Number Cultured | Number Positive | Per Cent Positive | I | II | IIa | Polyvalent* |
| March 20-21 (before treatment) | 100 | 36 | 36.0 | 22 | 3 | 0 | 11 | 100 | 38 | 38.0 | 20 | 1 | 1 | 16 |
| March 31-April 1 | 98 | 3 | 3.1 | 3 | 0 | 0 | 0 | 96 | 29 | 30.0 | 12 | 0 | 2 | 15 |
| April 7-8 | 96 | 2 | 2.1 | 1 | 0 | 0 | 1 | 98 | 56 | 57.1 | 32 | 0 | 2 | 22 |
| April 14-15 | 98 | 2 | 2.0 | 1 | 0 | 0 | 1 | 96 | 49 | 51.0 | 26 | 1 | 2 | 20 |
| April 21-22 | 97 | 7 | 7.2 | 2 | 1 | 1 | 3 | 96 | 55 | 57.2 | 29 | 1 | 3 | 22 |
| May 20-31 | 147 | 8 | 5.4 | 2 | 1 | 2 | 3 | 147 | 82 | 55.8 | 51 | 6 | 6 | 19 |

* Includes micro-organisms which have biologic reactions of meningococci and agglutinate in polyvalent antimeningococcus horse serum but which do not agglutinate in group specific antimeningococcus rabbit serums.

TABLE 2.—*Incidence of Meningococcus Carriers in Treated and Control Groups*

Fort B, April 6-May 27, 1943

| | Treated Group | | | | | | | Control Group | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Meningococcus Grouping | | | | | | | Meningococcus Grouping | | | |
| Date of Culture | Number Cultured | Number Positive | Per Cent Positive | I | II | IIa | Polyvalent* | Number Cultured | Number Positive | Per Cent Positive | I | II | IIa | Polyvalent* |
| April 6-7 (before treatment) | 100 | 30 | 30.0 | 12 | 0 | 4 | 14 | 100 | 29 | 29.0 | 10 | 2 | 0 | 17 |
| April 13-14 | 100 | 0 | 0.0 | 0 | 0 | 0 | 0 | 100 | 43 | 43.0 | 19 | 7 | 3 | 14 |
| April 27-28 | 97 | 2 | 2.1 | 2 | 0 | 0 | 0 | .. | .. | .... | .. | .. | .. | .. |
| May 4-5 | .. | .. | ... | .. | .. | .. | .. | 95 | 28 | 29.5 | 15 | 4 | 4 | 5 |
| May 26-27 | 97 | 0 | 0.0 | 0 | 0 | 0 | 0 | 48 | 16 | 33.3 | 7 | 4 | 0 | 5 |

* Includes micro-organisms which have biologic reactions of meningococci and agglutinate in polyvalent antimeningococcus horse serum but which do not agglutinate in group specific antimeningococcus rabbit serums.

Because additional studies undertaken at Camp A had suggested that smaller doses of sulfadiazine might also be effective as a prophylaxis in cerebrospinal fever, all individuals in the treated group in the N Division were given at the same time 1 Gm. of sulfadiazine by mouth twice daily for two days. The drug was issued to the men as they entered the mess halls for breakfast and supper. Treatment started on the evening of April 7 and was completed on the morning of April 9. Precautions similar to those at Camp A were taken to ascertain that each man swallowed the tablets. In this instance, however, no instructions regarding possible toxic symptoms were given, since it seemed desirable to observe the treated group without introducing the factor of suggestion.

At intervals subsequent to the completion of prophylactic treatment, meningococcus carrier studies were undertaken in the treated and control groups. As at Camp A, the nasopharyngeal cultures were obtained each time from the same men originally included in the carrier surveys. The results of these observations are set forth in table 2. These findings are essentially the same as those observed at Camp A in that the prophylactic administration of sulfadiazine by mouth appreciably reduced the meningococcus carrier rate among the men who received the drug.

4. One of these men had been admitted to the Station Hospital for measles. Nine days after admission, while still hospitalized, he developed meningitis. The other man was transferred to an untreated organization three weeks after he had received the drug. Fourteen days after transfer, signs of meningitis appeared.

The administration of 2 Gm. of sulfadiazine daily for two days apparently caused very few toxic symptoms among the 7,000 treated men in the N Division. There was no interference with the scheduled basic training program during the period of treatment. Indeed, the questioning of a large number of men by regimental medical officers and the staff of the Fourth Service Command Laboratory failed to reveal the occurrence of any definite toxic effects. It will be remembered that efforts were made to eliminate the factor of suggestion during the treatment of this group. Blood sulfadiazine levels, obtained at random from 20 men two hours after the third dose of sulfadiazine and eight hours after the last dose, ranged from 2.7 to 5.4 per hundred cubic centimeters by the method of Bratton and Marshall.[3]

## COMMENT

These data indicate that the prophylactic administration of sulfadiazine by mouth, even in relatively small doses, is a safe and effective method for curbing epidemics of meningococcic meningitis among large numbers of troops. This method of prophylaxis might also prove to be of value in terminating outbreaks of this disease in other situations, for example on troop transports at sea or in schools, orphanages and other institutions.

In these studies the drug was given at one and the same time to all members of the groups to be treated. It should be emphasized that these were closed groups in which there was little opportunity for the usual fortuitous reinfection from outside sources to occur. It seems probable that the effectiveness of the prophylaxis described herein depended on (1) treating all individuals in the group simultaneously, (2) treating all personnel who joined the group subsequent to the institution of prophylaxis before they were incorporated into the group and (3) keeping the treated group closed to reinfection from outside sources.

## SUMMARY

1. Sulfadiazine was administered prophylactically to more than 15,000 soldiers in residence at two posts where meningococcic meningitis was particularly prevalent during the spring of 1943. In one instance 3 Gm. of drug was given by mouth daily for three days; in the other the dose was 2 Gm. daily for two days.

2. Following the institution of prophylactic therapy the incidence of cerebrospinal fever among the treated individuals fell abruptly. Only 2 cases of the disease occurred during a subsequent period of eight weeks of observation. At the same time 40 cases were found among 18,800 untreated controls.

3. Meningococcus carrier surveys showed that the administration of sulfadiazine by mouth effectively lowered the carrier rate in the treated group at a time when the incidence of carriers among the untreated controls remained high or actually increased.

4. No serious toxic reactions resulted from the large scale administration of the drug. The treated men continued their usual daily activities without interruption of the scheduled basic training program during the period of treatment.

# *Clinical Notes, Suggestions and New Instruments*

## A CASE OF STAPHYLOCOCCIC ACTINOPHYTOSIS (BOTRYOMYCOSIS) IN MAN

### THE TENTH REPORTED HUMAN CASE

CHARLES H. DRAKE, PH.D.; MERVIN T. SUDLER, M.D., PH.D., AND RALPH I. CANUTESON, M.D., LAWRENCE, KAN.

At the present time the rapid advances in chemotherapy make it increasingly important to identify precisely the etiologic agents of infections, since in many cases the selection of a chemotherapeutic drug for treatment is as dependent on the nature of the infecting organism as it is on the clinical picture of the disease. With this in mind we believe it might be of value to report a case of a rare infection in man and point out the ease with which the disease can be misdiagnosed.

T. S. V., a white man aged 21, married, a medical student, consulted a physician in the clinic on June 5, 1943 about a small mass near the anus, present for about two months and uncomfortable only in certain sitting positions. He knew of no injury to the area.

Examination showed a mass about 10 mm. in diameter situated in the fatty tissue of the perineum just medial to the tuberosity of the left ischium, and a smaller one medial to this but with no demonstrable connection with the anus. The superficial skin was mildly reddened over the larger mass. The mass was easily circumscribed and only slightly tender. Rectal examination gave no additional information.

The impression was that this was an infected sebaceous cyst and the patient was advised to use hot compresses over the area affected.

On June 12 he was seen again. There was no localization of the infection. He was hospitalized for hot compresses, because he was uncomfortable sitting in class and had poor facilities for treatment at his home. His temperature was normal. The white blood count was 9,600 with 67 per cent polymorphonuclear cells, 30 per cent lymphocytes, 1 per cent monocytes and 2 per cent eosinophils.

On June 14 the mass was incised, yielding about 2 drachms of granular sanguinopurulent drainage. Recovery was rapid. He was dismissed from the hospital on June 16 with the incision closed. There has been no recurrence to date.

Pus removed from the abscess at operation was examined at the department of bacteriology and found to contain small white granules about half again as large as a pinhead. Under the microscope these granules were coarsely lobulated and the surface was covered with tightly packed clublike projections. Under both the low and high powers of the microscope the granules appeared identical with the sulfur granules observed in actinomycosis when they were examined either as fresh mounts or after treatment with 20 per cent potassium hydroxide solution. Gram stains were prepared from a crushed granule but instead of showing the characteristic fragments and fine, branched, gram-positive mycelium as are found in true sulfur granules, only masses of staphylococci were present. Smears from a number of the granules yielded the same results, but a careful examination of smears prepared from the pus surrounding the granules showed only a few staphylococci after long examination. The cells present were considerably disintegrated and consisted chiefly of polymorphonuclear neutrophilic leukocytes and considerable numbers of mononuclear cells. The presence of granules composed of masses of staphylococci, with few of the bacteria found outside the granules, identifies the infection as staphylococcic actinophytosis, or botryomycosis. Cultures from the crushed granules yielded a pure culture of Staphylococcus aureus. This was somewhat less pigmented than usual and showed no hemolysis on blood agar but was coagulase positive and gave the usual cultural reactions.

From the Department of Bacteriology, University of Kansas School of Medicine (Dr. Drake), and the Watkins Memorial Hospital, University of Kansas (Dr. Sudler, consultant in Surgery, and Dr. Canuteson, director, Student Health Service).

Botryomycosis was described by Bollinger[1] in 1870 as a disease of horses, usually following castration by crude methods, characterized by a granulomatous lesion that slowly involves the surrounding tissues but only rarely becomes generalized. In pus discharged from the lesion the causative organism occurs as small, lobulated and frequently clubbed granules which were believed to be mycotic in nature and were assigned to the genus Botryomyces. The infection has also been reported in other animals.[2]

The true nature of the disease was shown by Magrou[3] in 1914. This author carried out a complete investigation which showed that the causative organism was Staphylococcus aureus, identical in all respects with ordinary strains of the bacterium but which occurred in the tissues in the form of peculiar granules rather than scattered throughout the pus as in ordinary staphylococcic infections. Magrou showed that these granules were composed of masses of staphylococci embedded in a matrix and were usually surrounded by some kind of membrane. The periphery of the granules, which were usually lobulated, was frequently covered by closely packed clubs as in the sulfur granules of actinomycosis. He pointed out that the lesions in horses usually contained horsehairs as foreign bodies and was able to reproduce the disease in rabbits and guinea pigs by inserting into the testes horsehair contaminated with staphylococci. Further work showed that foreign bodies were not absolutely necessary but that the disease could be produced in experimental animals by the injection of small numbers of Staphylococcus aureus. It was necessary to have the number of organisms within a definite range so that there were too few to produce a purulent inflammation but yet sufficient so that they would not be absorbed with little or no tissue reaction. Once the correct range has been established for any culture, the disease could be produced at will both with cultures isolated from botryomycosis and with ordinary strains of staphylococci.

In his paper, Magrou recorded from the literature (Kaiser and Gryns) one probable human case of botryomycosis occurring as an osteomyelitis. Since that time 8 other human cases have been recorded. Masson[4] in 1918 reported a second case in man, also occurring as an osteomyelitis, following a hip fracture by a shell fragment. Two cases of nontraumatic osteomyelitis of botryomycotic nature were reported by Fumagalli[5] in 1928. Berger and his associates[6] reported the fifth case in 1936 and the first case in which the infection was confined to soft tissues, occurring as an infection of the genital tissues of a woman. They also point out that a much more common infection in man, granuloma telangiectaticum, has erroneously been called botryomycosis and, since in addition the true disease is not a mycosis, suggest that the infection might better be termed "staphylococcic actinophytosis." The sixth human case was observed by Plaut[7] in 1937 as an abscess of the abdominal wall, which contained a broom straw in addition to the typical granules. The seventh and eighth cases were observed by Kimmelstiel and Oden[8] in 1939 as abdominal abscesses, both of which contained fragments of fish bones. One of these cases was admitted by the authors to be questionable. The ninth case was recorded in 1941 by Fink[9] as a liver abscess with involvement of the lung by both direct extension and metastases.

It would appear from the small number of reported cases that the disease is rare in man, but there can be little doubt that this rarity is more apparent than real. Of the recorded cases several have been diagnosed only by the examination of tissues removed at autopsy or at operation, so that many cases are no doubt missed. This infection can readily be confused with actinomycosis or may be dismissed as a simple, chronic, inflammatory process. The granules are usually quite small and readily overlooked unless the pus is carefully examined with the naked eye. Simple smears of the exudate are unlikely to contain the granules, so that there can be little doubt that in many cases the granules have been overlooked. Plaut especially points out the importance of differentiating between botryomycosis and actinomycosis, since the prognosis is more favorable in botryomycosis and less radical treatment is necessary. This is borne out by our case, which responded readily to simple drainage. Of the reported infection involving only soft tissues, Berger's patient was still alive twenty months after the onset although unimproved, Plaut's patient recovered rapidly after operation, one of Kimmelstiel and Oden's patients died of complications following operation but the other was completely cured one month after operation, and Fink's patient died from a generalization of the infection but the disease was not diagnosed until autopsy.

Confusion in diagnosis would arise from observation of the granules in fresh material since they are almost identical under low and high powers of the microscope with the granules observed in actinomycosis. It is essential that crushed granules be examined by means of the gram stain. This procedure readily shows that the granules are composed of staphylococci rather than the branched, fine, gram-positive mycelium that makes up the sulfur granules of true actinomycosis. This procedure should never be neglected, since this is necessary to differentiate between the granules of staphylococcic actinophytosis, actinobacillosis, actinomycosis and mycetoma. In staphylococcic actinophytosis the granules are composed of masses of staphylococci embedded in a matrix of some kind and are usually surrounded by a refringent membrane the surface of which is often bedecked with clubs. Occasionally granules from old lesions are calcified. The nature of the matrix and of the limiting membrane are the subject of some dispute. Some authors believe that either or both materials arise from the organisms, probably from proteins derived from disintegrated bacteria. However, others believe that either or both of these substances arise from the host tissues. In some cases it would appear that the hard membrane described was due to calcification. Kimmelstiel and Easley[10] claim to have produced the disease in experimental animals and to have traced the development of the matrix from disintegrating tissue elements. This problem, however, is common to the formation of club covered granules in all of the diseases mentioned and need not be considered here in any detail.

Even considering the fact that many cases of this disease are probably overlooked, it still seems to be less common in man than in lower animals and especially the horse. This is rather surprising in view of the fact that staphylococcic infections are more common in man than in the lower animals. Although Magrou considered that the natural development of the disease was primarily due to infection with a limited number of organisms, this view has been questioned by several authors, who point out that man is frequently, if not more frequently, exposed to infection with a limited number of staphylococci. The importance of foreign bodies has been stressed by a number of workers, and their importance in the development of experimental infections has been shown by Kimmelstiel and Easley. In at least 7 of the reported cases in man, foreign bodies, such as bony sequestrums, fish bones and a broom straw, have been found in the lesions.

We would suggest, at present on purely theoretical grounds, that the development of the disease is dependent on a careful balance between the defense mechanisms of the host and the invasive powers of the organisms. Several workers have pointed out the rather low virulence for experimental animals shown by cultures of Staphylococcus aureus isolated from staphylococcic actinophytosis. In our case the organisms presented the anomalous characteristic of lack of hemolytic powers but was still coagulase positive, as is characteristic of most pathogenic strains. This lower virulence is a point in favor of our theory, as is the fact that the infection is more common in animals possessing a higher natural resistance to staphylococci than that shown by man. The disease probably develops as a result of the entrance into the tissues of staphylococci of low invasive powers but which are able to maintain themselves

1. Bollinger, O.: Virchows Arch. f. path. Anat. **49**: 583, 1870.
2. Aynaud, M.: Ann. Inst. Pasteur **42**: 256, 1928, cited by Berger.[6]
3. Magrou, J. E.: Les grains botryomycotiques, Thesis 267, Paris, 1914.
4. Masson, P.: Lyon chir. **15**: 230, 1918, cited by Berger.[6]
5. Fumagalli, R. C.: Ann. d'anat. path. **4**: 513, 1927, cited by Berger.[6]
6. Berger, Louis; Vallée, Arthur, and Vézina, Charles: Genital Staphylococcic Actinophytosis (Botryomycosis) in Human Beings, Arch. Path. **21**: 273 (March) 1936.
7. Plaut, Alfred: Botryomycosis in Man, Arch. Path. **23**: 602 (April) 1937.
8. Kimmelstiel, Paul, and Oden, P. W.: Botryomycosis: Report of Two Cases of Intra-Abdominal Granuloma, Arch. Path. **27**: 313 (Feb.) 1939.
9. Fink, A. A.: Staphylococcic Actinophytotic (Botryomycotic) Abscess of the Liver with Pulmonary Involvement, Arch. Path. **31**: 103 (Jan.) 1941.
10. Kimmelstiel, Paul, and Easley, C. A., Jr.: Experimental Botryomycosis, Am. J. Path. **16**: 95 (Jan.) 1940.

there, often aided by the presence of foreign bodies. This would cause the formation of a chronic inflammatory process with a purulogranulomatous tissue reaction. It is a fundamental peculiarity that all of the infections characterized by the growth of the organisms in granules are also characterized by at least a partially granulomatous tissue reaction.

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## TREATMENT OF VINCENT'S ANGINA OF THE TONSIL

### A PRELIMINARY REPORT

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The great number of methods and combinations of drugs used by various clinicians in treatment of Vincent's angina indicates that none of them have proved entirely satisfactory. It is a common experience, whether infection is present in the gums or in the pharynx, to have these patients returning frequently over a long period of time. An apparent cure within a period of ten days is usually considered quite satisfactory, and even then, owing to frequent recurrences, the wise clinician avoids assuring his patient that he is completely cured.

The fusiform organisms and spirochetes of Vincent's angina have many of the characteristics of a secondary invader. It is commonly believed that these organisms enter only into tissues weakened by some other cause. What this cause is has not definitely been determined, but there is some evidence that nutritive factors play a part. It is also possible that some associated infection may prepare the ground.

Vincent's infection of the tonsil was seen recently in several soldiers returning from the South Seas. These men had been exposed to strenuous physical conditions for a considerable period of time with meager rations while on front line duty. They were all sent back to the zone of the interior with various types of disability. On account of the likelihood of a pronounced increase of cases of this type under war conditions, it is considered advisable to make this preliminary report showing remarkable recovery under treatment with sulfathiazole. The first 2 patients had initial treatment with other methods without effective results. Each patient reported definite improvement in soreness of the throat within twenty-four hours, with most symptoms gone in forty-eight hours and practically complete clinical recovery within seventy-two hours under treatment with sulfathiazole.

The dosage and method of administration ultimately used consisted of a 0.5 Gm. sulfathiazole tablet dissolved on the tongue every two hours during the day and 1 Gm. dissolved on the tongue every four hours during the night. This was continued for two days, at which time the patient would voluntarily discontinue medication, unless directed otherwise, because symptoms had disappeared. When infection also was present about the gum margins, it was advised that the sulfathiazole tablet be moistened with a few drops of water to make a paste and this used to rub into the gum margins. Excellent results were secured on the gums in 1 case using this method, but it was not tried sufficiently to warrant any expression of opinion.

A search of the literature fails to reveal any use of sulfonamide drugs for this purpose, except 1 case treated by Pelner.[1] A remarkable cure was secured with azosulfamide. However, Spink in his book on "Sulfanilamide and Related Compounds" states that sulfanilamide has been used in treatment of gingival infections such as pyorrhea and Vincent's angina with no benefit from local or oral administration.

### REPORT OF CASES

CASE 1.—E. E. B. A man aged 26, was sent in with a sore throat of seven days' duration and a grayish membrane on the tonsil. Microscopic examination showed great masses of fusiform bacilli and spiral forms from the necrotic area. He was given 0.045 Gm. of mapharsen intravenously and local treatment to the tonsil consisting of aqueous 10 per cent mercurochrome. I had previously secured excellent results by using neoarsphenamine intravenously but at this time the drug was not available. The patient returned in two days with the throat still very sore, and local treatment with silver nitrate and mercurochrome was given. The same treatment was repeated the following two days, and, owing to some ulceration of the gum margin anteriorly, it was advised that sodium perborate paste be massaged into the gums three times daily. On the fifth day little improvement was noted in the condition, so it was decided to give sulfathiazole orally, 1 Gm. every four hours, in addition to local treatment. The throat was much improved the following day and after forty-eight hours recovery was sufficiently complete to warrant stopping treatment. Some ulceration of the gum margins remained. It was advised to continue sodium perborate paste for two or three days. Tonsillectomy was done under local anesthesia in about another week.

CASE 2.—S. W. S., a boy aged 13 years, received with a diagnosis of membraneous pharyngitis of three days' duration, gave no previous history of sore throat but had suffered from dry cough for about one week. A smear from the tonsils showed large numbers of fusiform organisms and spirals of Vincent's angina. He was first seen on March 26, 1943 and given intravenously 0.045 Gm. of mapharsen, and sodium perborate paste to the gum margins. After four days there was still some soreness and some membrane present. After several days more of local treatment there was gradual recovery. On April 13 there was an acute recurrence of the infection in both tonsils. Another intravenous injection of mapharsen was given, as well as local treatment to the affected areas. On April 18 infection was still present and sulfathiazole 1 Gm. every four hours, to be dissolved on the tongue, was ordered for two days. Two days later the patient was seen and had no complaints. Ulcerations had disappeared and there was no soreness in the tonsils, although there was still some infection in the gum margins. Tonsillectomy was done two days later with good results.

CASE 3.—C. J. L., a man aged 23, who complained of sore throat for about ten days had a deep ulceration in the middle of the left tonsil. A smear from this area showed many fusiform organisms and spirals of Vincent's angina. The treatment consisted only of sulfathiazole 0.5 Gm. on the tongue every two hours during the day and 1 Gm. every four hours during the night for two days. The patient failed to return as directed. He was looked up after six days and it was found that he had felt well after two days and saw no need for returning. He was much improved after twenty-four hours. In order to prevent recurrence he was advised to take a high vitamin diet, including considerable orange or grapefruit juice, greens and brewers' yeast.

CASE 4.—B. N., a youth aged 20, complained of sore throat of two days' duration. An ulcerated area was present in the right tonsil and there was much ulceration of the gum margins. A smear from the tonsil showed numerous fusiform organisms and spirals of Vincent's angina. The gum margins would bleed profusely from the slightest touch. He was first seen on May 18, 1943 and given sulfathiazole 0.5 Gm. dissolved on the tongue every two hours during the day and 1 Gm. every four hours during the night. The next day he was much improved, with the soreness of the throat much better and the ulceration in the tonsils and gum margins apparently much improved. On the third day no soreness remained and the throat and gum margins appeared practically healed.

On account of the probability of an increase in epidemics of this type due to war conditions and a lowering of the general nutritive condition in certain groups or areas, it is hoped that others will try this method of treatment where more cases are available for observation. In the cases reported, dietary advice or brewers' yeast were not given until the acute condition had been controlled.

The 4 cases reported are the first 4 cases treated with sulfathiazole. The very remarkable results suggest that it may be a specific cure for the condition, although it is impossible to draw any conclusions. It is believed that recurrences of the infection are likely to occur from any type of treatment unless factors which cause weakened resistance in the tissues are controlled.

1. Pelner, Louis: New York State J. Med. **41**: 1358 (July) 1941.

## Special Article

# HANDBOOK OF NUTRITION: XXIV

## NUTRITION IN PREVENTIVE MEDICINE

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*(Concluded from page 287)*

### VITAMIN $B_1$ (THIAMINE) DEFICIENCY

Vitamin $B_1$ (thiamine) deficiency has been known since antiquity by many synonyms: polyneuritis endemica, barbiers (France), loempoe (Java), kakke (Japan and China), taon (Philippines), maladie des sucréries (French Antilles), hinchazon (Cuba), michasas or pernieras (Brazil), maladie des jambes (Louisiana).[109]

The classic type of beriberi is characterized by symptoms due to damage of the nervous and cardiovascular systems and produces neuritis and heart failure. In the so-called "dry" type of the disease the nervous manifestations are the predominant symptoms, and in the "wet" type the edema of heart failure is the more striking sign. Various combinations may exist. The neuritic form is seen most commonly in the United States[110] except in some areas of Louisiana, where classic beriberi occurs.[111] Infantile beriberi occurs in breast fed infants of mothers with the disease.

Geographically the disease is widespread, occurring endemically or sporadically in all parts of the world. The classic form is common in Asia and Australasia. It occurs with less frequency in Africa, South and Central America, Europe and the United States (table 5). In the latter country about 20 per cent of chronic alcoholic addicts have neuritic manifestations of the disease.[110] Infantile beriberi has a death rate of over 90 per cent and is a chief cause of infant death in the Far East.[112]

### NICOTINIC ACID DEFICIENCY (PELLAGRA)

Deficiency in niacin (nicotinic acid) or closely related substances results in the disease pellagra. The most prominent symptoms of pellagra are stomatitis, dermatitis, mental changes, gastrointestinal upsets and weakness. Pellagra occurs most commonly in people of poor economic status because of the greater food restrictions in this group. In the United States most of the cases occur in the Southeastern states in the spring and early summer.

From 1933 to 1940 the annual death rates from pellagra in thirteen states of the Southeastern United States varied between 5.1 to 22.4 per hundred thousand of population.[113] In 1941, four years after the discovery that nicotinic acid was the pellagra preventive vitamin, 1,868 deaths were reported from pellagra in the United States.[114] Many other reports offer strong evidence that pellagra remains prevalent in the United States. Bean, Spies and Blankenhorn[115] estimate that 1 to 2 per cent of all admissions to the medical services of the Lakeside Hospital, Cleveland, and the Cincinnati General Hospital were due to pellagra. Goldsmith[116] found evidence of pellagra in 17 per cent of 200 consecutive admissions to the medical services of the Charity Hospital, New Orleans. Many other reports of cases of pellagra both within and without the endemic areas in the United States are summarized in table 6.

Outside the United States the great endemic areas appear to be Egypt, Rumania, Bulgaria and many parts of Africa. Ellinger, Hassan and Tahá[117] found that 34.3 per cent of 204 people examined in lower Egypt had signs of pellagra; Clark[118] states that 201 cases were admitted to the dermatologic service of the Alexandria Hospital in 1931-1933 and that the incidence at the Cairo General Hospital was 3 to 24 cases per thousand admissions to the medical services. In 1918, 70,000 cases were said to exist in Rumania,[119] and in 1934 the death rate in Rumania is given as 11.8 per hundred thousand of population.[120] The data on Bulgaria are not so definite, but Molov[121] believes that pellagra is the most common avitaminosis in that country. Trowell[122] states that pellagra is endemic among the children in certain tribes on the east and west coasts and in Central Africa. Nauck[123] makes the astonishing estimate that in Transcaucasia in 1933 there were 30,000 to 50,000 pellagrins in a population of 1,300,000, or a case incidence of 23 to 38 per cent. Alessandri and his collaborators[124] estimated the number of cases in Chile in 1942 to be 3,000. Smaller numbers of cases have been reported from India,[125] Russia,[126] China,[127] Japan,[128] South America,[129] and many of the British colonies.[119] Exclusive of Spain, Italy and the Balkans, the disease seems to be only sporadic in Europe.

### ARIBOFLAVINOSIS

Ariboflavinosis is a disease due to deficiency of the water soluble vitamin riboflavin. It is characterized by the development of cracks in the skin at the corners of the mouth (cheilosis), a greasy eruption of the skin, changes in the tongue and keratitis, caused by an invasion of the cornea by blood vessels.

Because of the recent description of the disease, information on its incidence is relatively scanty. In

109. Williams, R. R., and Spies, T. D.: Vitamin $B_1$ (Thiamine) and Its Use in Medicine, New York, Macmillan Company, 1938.

110. Scott, L. C., and Herrmann, G. R.: Beriberi ("Maladie des Jambes") in Louisiana, J. A. M. A. **90:** 2083 (June 30) 1928.

111. Jolliffe, Norman: Quart. J. Studies on Alcohol **1:** 74 (June) 1940.

112. Beckman, Harry: Treatment in General Practice, Philadelphia, W. B. Saunders Company, 1930.

113. De Kleine, William: South. M. J. **35:** 992 (Nov.) 1942; Am. J. Pub. Health **27:** 595 (June) 1937.

114. Division of Sanitary Reports and Statistics, U. S. Public Health Service, personal communication to the author.

115. Bean, W. B.; Spies, T. D., and Blankenhorn, Marion A.: The Incidence of Pellagra in Ohio Hospitals, J. A. M. A. **118:** 1176 (April 4) 1942.

116. Goldsmith, Grace A.: South. M. J. **36:** 108 (Feb.) 1943.

117. Ellinger, P.; Hassan, A., and Tahá, M. M.: Lancet **2:** 755 (Sept. 25) 1937.

118. Clark, Alfred: J. Trop. Med. & Hyg. **40:** 221 (Oct. 1) 1937.

119. Stannus, H. S.: Trop. Dis. Bull. **33:** 729 (Oct.) 1936.

120. Jonesco-Mihaiesti, C.; Cuica, A., and Cuica, M.: Arch. Roumaines de path. exper. et microbiol. **8:** 422, 1932.

121. Molov, V.: Liječn Vjern. **59:** 397, 1937; abstr. Zentralbl. f. d. ges. Hyg. **41:** 409, 1938.

122. Trowell, H. C.: Arch. Dis. Childhood **12:** 193 (Aug.) 1937.

123. Nauck, E. G.: Beihefte z. Arch. f. Schiffs- u. Tropen-Hyg. **37:** 85, 1933.

124. Alessandri, H.; Garcia Palazuelos, P., and Lerner, M. J.: Rev. argent. d. Dermatosif. **26:** 25, 1942.

125. Aykroyd, W. R.: Bull. Off. internat. d. hyg. pub. **29:** 2388, 1939. Batra, B. L.: Indian M. Gaz. **77:** 269 (May) 1942. Carruthers, L. B.: Tr. Soc. Roy. Med. & Hyg. **35:** 21, 1941. Raman, T. K.: Indian J. M. Research **27:** 743 (Jan.) 1940. Ahmed, N.: Indian M. Gaz. **77:** 140 (March) 1942. Sen Gupta, P. C.; Rai Chaudhuri, M. N.; Chaudhuri, R. N., and Napier, L. E., ibid. **74:** 143 (March) 1939. Ahmed, N.: J. Indian M. A. **12:** 1 (Oct.) 1942. Goodall, J. W. D.: Indian M. Gaz. **75:** 147 (March) 1940. Napier, L. E., ibid. **74:** 137, 1939.

126. Wyjasnowsky, J.: Arch. f. Schiffs- u. Tropen-Hyg. **38:** 31, 1934.

127. Yang, C. S., and Huuang, K. K.: Chinese M. J. **48:** 701, 1934. Yu, K. Y., ibid. **48:** 724 (Aug.) 1934. Wilson, R. M., ibid. **39:** 661, 1926. Morris, H. H.; Hwang, M. S., and Kuo, P. T., ibid. **57:** 427, 1941. Urabe, K.: Jap. J. Dermat. u. Urol. **47:** 2, 1940.

128. Itoh, N.: Far East. Assn. Trop. Med., Tr. 6th Biennial Cong. Tokyo **1:** 315, 1925.

129. Da Costa, V. F., and Castro, M.: Rev. Assoc. paulista de med. **11:** 363, 1937. Bielltreich, R. A.: Rev. méd. latino-am. **26:** 351, 1941. Alessandri, Garcia Palazuelos and Lerner.[124]

1938 the Odens and Sebrell [130] felt that the disease might be common in the southern United States. Spies, Bean, Vilter and Huff [131] believe it to be the most common deficiency disease in the United States. Goldsmith [132] found an incidence of 34 per cent in 200 consecutive admissions to the medical services of Charity Hospital, New Orleans. Wiehl and Kruse [6] found that 75.8 per cent of pupils in a school in the East Side of New York City had signs of mild riboflavin deficiency, as did 34.4 per cent of a group of 143 WPA employees. Kruse's figures must be interpreted with care, since the diagnoses were made entirely on the changes found in the eyes, which by themselves are not specific of riboflavin deficiency. Nevertheless the reports cited plus additional ones cited in table 7 warrant the conclusion that the disease occurs in many parts of the United States and is very prevalent in the South.

Reports from other parts of the world are even more fragmentary than those from the United States. The disease has been reported in England [133] and is probably widespread in India,[134] China,[135] Malaya [136] and Africa.[137]

TABLE 5.—*Reports of Vitamin $B_1$ (Thiamine) Deficiency*

| Location | Comment | References |
|---|---|---|
| **AFRICA** | | |
| Brazzaville | Report of 12 cases in 1942 | Nicol, R.: Rev. sc. méd. Afrique Fr. **1**: 81, 1942 |
| Eastern Congo | Report of 50 cases in 1940 | Wilcoks, C.: Trop. Dis. Bull. **37**: 751, 1940 |
| 18th Mil. Reg. Fr. | 430 cases observed, 1929-1936 | Malard, M., and Delprat: Rev. Service de San. & Mil. **106**: 91, 1937 |
| Madagascar | Outbreak in some troops in 1937 | Sanner: Ann. méd. pharm. col. **36**: 840, 1938 |
| Nigeria | Common in famine years | Summary of Information Regarding Nutrition in the Empire, London, 1939 |
| **ASIA** | | |
| Burma | 1,564 cases in 1935 | McKinley, E. B.: Geography of Diseases, 1935 |
| Burma | Endemic | Youmans, J. B.: Nutritional Deficiencies, 1941 |
| Brunei | High incidence in parturient women and in children, 1935 | Ann. Rep. Med. Dept. (Brunei) 1935 |
| China | Endemic | Youmans, J. B.: Nutritional Deficiencies, 1941 |
| China (Shanghai) | 15 per cent of 760 hospital patients admitted for beriberi in 1939 | Kuo, P. T.: Chinese M. J. **55**: 427, 1939 |
| Hong Kong | 2.8 per cent of deaths due to beriberi in 1936 | Ann. Rep. Div. Med. & San. Service, 1936 |
| Hong Kong | 18 per cent of infants at a welfare center, 1941 | Fehily, Lydia: J. Trop. Med. & Hyg. **44**: 21, 1941 |
| Hong Kong | 1,661 deaths due to beriberi in 1938 | Summary of Information Regarding Nutrition in the Empire, London, 1939 |
| India | Endemic | Youmans, J. B.: Nutritional Deficiencies, 1941 |
| India (Guntur) | 510 cases (1926-1929) reported | Raman, T. K.: J. Indian Med. A. **12**: 50, 1942 |
| India (Vizagapatan) | 200 cases (1937-1940) reported | Raman, T. K.: J. Indian Med. A. **12**: 50, 1942 |
| India (Godavari) | Endemic | Aykroyd, W. R., and Krishman, B. G.: Indian J. Med. Res. **29**: 551, 1941 |
| India (Madras) | 40,000 cases per year (1941) | Aykroyd and Krishman, ibid. **29**: 703, 1941 |
| Indo-China | 3,365 cases in 1935 | McKinley, E. B.: Geography of Diseases, 1935 |
| North Borneo | Sporadic epidemics | Ann. Rep. M. Dept. (N. Borneo) 1936 |
| Trengganu | 1,176 cases treated in 1936 | Ann. Med. & San. Rept. (Trengganu) 1936 |
| Siam | 2,000 deaths per year | Bull. Health Off. League of Nations **9**: 361, 1940-1941 |
| **AUTRALASIA** | | |
| Australia | 8 per cent of 150 infants partially deficient, 1942 | Clements, F. W.: M. J. Australia, 1942 |
| Celebes | 3,000 cases, 1933-1934 | Fleischer, D.: Geneesk. Tijdschr. Nederl. Indië **75**: 1975, 1935; Abstr. Nutrition Abstr. & Rev. **6**: 184, 1936 |
| East Indies | 1,549 cases, 101 deaths in 1931; 1,333 cases, 129 deaths in 1932 | Indisch. Verslog., 1933. |
| Japan | Endemic | Youmans, J. B.: Nutritional Deficiencies, 1941 |
| Japan | 13,828 deaths in 1933; 11,841 deaths in 1934 | Ann. Rep. San. Bur. Imp. Jap. Gov., 1937 |
| Malay | Endemic | Youmans, J. B.: Nutritional Deficiencies, 1941 |
| Malay | 1,262 deaths in 1938 | Ann. Rep. of Med. Dept. (Malay), 1938 |
| Nauru | Endemic | Earle, K. V.: J. Trop. Med. & Hyg. **44**: 142, 1941 |
| New Guinea and Papua | 48 deaths in 1940 | U. S. Army M. Bull. No. 65 |
| New Guinea and Papua | Epidemics occur | Van Veen, A. G.: Bull. H. O. Leag. of Nations **9**: 357, 1940 |
| Philippines | 1935, 18,614 deaths; 1934, 21,419 deaths; 1933, 18,682 deaths; 1932, 17,173 deaths | Intergov. Conf. of Far Eastern Countries on Rural Hygiene, League of Nations, 1937 |
| Straits Settlements | 1,262 cases, 121 deaths in 1938 | Ann. Rep. Med. Dept. Straits Settlements, 1939 |
| **CENTRAL AMERICA** | | |
| Central America | Endemic | Beckman [112] |
| Costa Rica | 43 cases in 1939 | Bull. Off. San. for Pan. Am., 1939 |
| **EUROPE** | | |
| Balkans | Sporadic cases occur | McDougall, E. J.: Leag. of Nat. Health Org. Bull., 1939 |
| Hungary | Sporadic cases reported | Garanvolgyi, K.: Abstr. Nutrition Abstr. & Rev., 1936-1937 |
| Sardinia | Sporadic cases occur | Cocchi, C.: Rev. Clin. Pediat. **37**: 193, 1939 |
| St. Helena | 200 cases in 1938 | Summary of Information Regarding Nutrition in the Empire, London, 1939 |
| Iceland | 16 cases seen in 1933 | Kilka, P. V. G.: Laeknabl. 6/8, 18, 1933; Abstr. Nutrition Abstr. & Rev. **3**: 82, 1933 |
| **SOUTH AMERICA** | | |
| South America | Sporadic cases occur | Cecil, R. L.: Textbook of Medicine, 1942 |
| Brazil | Endemic | Zimmerman, H. M.: Nelson's Loose-Leaf Medicine |
| Argentina | Sporadic cases | Cossio, P., and Mola, B.: Dia méd. **9**: 1148, 1937 |
| British Guiana | Local epidemic 1934 | Report of Surg. Gen. (British Guiana), 1934 |
| **UNITED STATES and CARIBBEAN** | | |
| United States | 49 deaths in 1941 | U. S. Bureau of the Census, 1942 |
| United States | 20 per cent of alcoholic addicts | Jolliffe [111] |
| Louisiana | Endemic in certain areas | Scott and Herrmann [110] |
| West Indies | Occurs | Williams and Spies; [109] Beckman [112] |
| Trinidad | 87 cases in 2,422 consecutive admissions | Earle, K. V.: J. Trop. Med. & Hyg. **44**: 150, 1941 |

## VITAMIN C DEFICIENCY

Scurvy is a metabolic disease resulting from a deficiency of vitamin C and characterized by a general

130. Oden, J. W.; Oden, L. H., Jr., and Sebrell, W. H.: Pub. Health Rep. **54**: 790 (May 12) 1939.

131. Spies, T. D.; Bean, W. B.; Vilter, R. W., and Huff, W. E.: Am. J. M. Sc. **200**: 697 (Nov.) 1940.

132. Goldsmith, Grace A.: South. M. J. **36**: 108 (Feb.) 1943.

133. Scarborough, Harold: Brit. M. J. **2**: 601 (Nov. 21) 1942.

134. Aykroyd, W. R., and Kishnan, B. G.: Indian J. M. Research **24**: 411 (Oct.) 1936. Aykroyd, W. R., and Verma, O. P.: Indian M. Gaz. **77**: 1, 1942. Verma, O. P., ibid. **77**: 471 (Aug.) 1942.

135. Hou, H. C.: Chinese M. J. **59**: 314, 1941.

136. Laudor, J. V., and Pallister, R. A.: Tr. Roy. Soc. Trop. Med. & Hyg. **29**: 121, 1931.

137. Pursell, F. M.: Tr. Roy. Soc. Med. & Hyg. **35**: 323, 1942. Barlovatz, A.: Ann. Soc. belge de méd. trop. **21**: 13, 1940.

TABLE 6.—*Incidence of Pellagra*

| Area and Date | Incidence | References and Comment |
|---|---|---|
| 13 Southeastern states, U. S., 1922-1940 | Death rates per 100,000 population varied between 5.1 and 22.4 | De Kleine [113] |
| United States, 1933-1941 | Total deaths from pellagra in United States varied from 3,955 to 1,836 | Sanitary Reports [114] |
| Ohio Hospitals, U. S., 1942 | Pellagra accounted for 1 to 2% of admissions to medical wards | Bean, Spies and Blankenhorn;[115] noteworthy because outside endemic area |
| Charity Hospital, New Orleans, 1942 | Pellagra found in 17% of 200 consecutive admissions to medical wards | Goldsmith [116] |
| Charity Hospitals, New Orleans and Shreveport, La., 1937-1941 | 3 to 21 deaths yearly in these 2 hospitals | Lowe, R. C.: New Orleans M. & S. J. **95**: 407, 1943; 58 to 152 cases admitted yearly |
| Michigan, 1940 | Signs and symptoms of pellagra frequent in Northern states, especially in the alcoholic | Field, H., Jr.: New England J. Med. **223**: 307, 1940; states that disease is commonly overlooked in the north |
| California, 1928-1935 | Death rates varied from 0.72 to 1.36 per 100,000 population | Smith, C. E., and Stevens, I. M.: Am. J. Hyg. **27**: 590, 1938 |
| Indiana, 1934 | Reports 11 cases | Fouts, P. J., and Zerfas, L. G.: J. Indiana State M. A. **27**: 196, 1939; all cases admitted to Indianapolis General Hospital |
| Kentucky, 1939 | Reports 41 cases | Kooser, J. H., and Blankenhorn, M. A.: J. A. M. A. **112**: 2581, 1939; all cases occurred in county (Perry) |
| Alabama, 1937 | 50 cases admitted to Hillman and T. C. I. Hospitals, Birmingham | Spies, T. D.: Chinn, A. B., and McLester, J. B.: J. A. M. A. **108**: 853, 1937 |
| Alabama, 1939 | Reports 977 cases of multiple B vitamin deficiency (see riboflavin table) | Spies, T. D.; Vilter, R. W., and Ashe, W. F.: J. A. M. A. **113**: 931, 1939; states that multiple deficiency states are very common |
| Canada, 1942 | Reports 1 case | Quentin, T. J.: Canad. M. A. J. **47**: 464, 1942 |
| England and Wales, 1928-1938 | 77 deaths reported in 10 year period | Registrar General's Statistical Review of England and Wales for the years 1938, New Annual Series, No. 18, H. M. Stationery Office, London |
| Northern Ireland, 1942 | 16 cases | Deeny, J.: Brit. M. J. **1**: 157, 1942; 16 patients with suggestive skin or gastric symptoms were relieved with niacin |
| England, 1934-1939 | 8 cases | Davies, J. H. T., and McGregor, H. G.: Brit. J. Dermat. & Syph. **51**: 51, 1939 |
| England, 1941 | 1 case | Davis, E., and Hinden, E.: Lancet **1**: 10, 1941: patient was alcoholic |
| Scotland, 1940 | 1 case | Robertson, D. S.: Edinburgh M. J. **47**: 81, 1940 |
| Italy, 1937 | 74 deaths in 1937 | Statistica delle Cause di Morte nell'Anno 1937 |
| Transcaucasia, 1933 | 30,000 to 50,000 cases estimated | Nauck;[123] total population, 1,300,000 |
| Bulgaria | Author saw personally 223 cases in 35 years of practice | Molov;[121] the most important avitaminosis in Bulgaria is pellagra |
| Rumania, 1918 | 70,000 cases estimated | Stannus;[119] source of figure is not clear in reference |
| Belgium, 1939 | 1 case | Van Bogaert, L., and Vanden Berghe: Bull. Acad. roy. di méd. Belgique **4**: 409, 1939 |
| Switzerland, 1938 | 2 cases | Bickel, G.: Schweiz. med. Wchnschr. **68**: 1159, 1938 |
| Norway, 1934-1939 | 18 cases | Kielland, J.: Nordisk. Med. **1**: 663, 1939 |
| Netherlands, 1938 | 10 cases | DeLangen, C. D.; Bowsijk, J. C., and van Nieuneuhuizen, C. L. C.: Nederl. tjdschr. v. geenesk. **72**: 4970, 1938 |
| Sweden, 1939 | 5 cases | Mindus, E.: Nordisk. Med. **3**: 2477, 1939; "many ill defined cases seen" |
| Germany, 1939 | 1 case | Salm, H.: München. med. Wchnschr. **86**: 882, 1939 |
| Spain, 1937-1938 | "Many" in Madrid during and after Spanish Civil War | Jiminez; Garcia, F., and Grande Covian, F.: Rev. clin. española, **1**: 313, 1940 |
| Rumania, 1934 | Death rate 11.8 per 100,000 | Jonesco-Mihaiesti, Cuica and Cuica [120] |
| Rumania (Moldovia), 1938 | 2 cases in 4 families comprising 33 persons | Enescu, M., and Rodenschi, A.: Abstr. Zentralbl. f. d. ges. Hyg. **41**: 250, 1938 |
| Brazil, 1930-1937 | 114 cases at Recife, 16 cases in rest of Brazil | Da Costa and Castro [129] |
| Argentina, 1941 | 8 cases reported to 1941 | Bielltreich;[129] pellagra is rare in Argentina |
| Chile, 1942 | 110 cases reported in Santiago | Alessandri [124] states that there are now 3,000 cases in Chile |
| Africa, 1937 | Describes 26 cases occurring in 1934-1935 in Nairdii Hospital, Kenya Colony in children | Trowell [122] states that the disease is endemic on east and west coasts and in Central Africa |
| Africa, 1932-1933 | 145 total | Stannus;[119] figures collected from annual medical reports of colonies |
| Africa, 1937-1938 | 171 cases at Aba and Lagos, Nigeria, in 744 persons examined | Moore, D. F.: J. Trop. Med. & Hyg. **42**: 109, 1939 |
| Egypt, 1937 | Found pellagra in 34.3% of 204 people examined in lower Egypt | Ellinger; Hassan and Tahá;[117] pellagra is rare in upper Egypt but does occur |
| Egypt, 1931-1933 | Rate at Cairo General Hospital was 3 to 24 cases per 1,000 admissions, depending on the season | Clark [118] |
| Egypt, 1938 | 15 cases | Alport, A. C.; Chalioungui, P., and Hanna, G.: Lancet **2**: 1460, 1938 |
| India | Pellagra is very frequent in a large percentage of infants | Aykroyd [125] |
| India, 1942 | Widespread | Batra;[125] all types of deficiency disease are seen, but pellagra is most widespread |
| India, 1941 | Describes 10 cases | Carruthers [125] |
| India, 1940 | Describes 25 cases; incidence 0.65% of admissions to medical wards | Raman;[125] Vizagapatam is an endemic focus of pellagra |
| India, 1942 | Saw 6 cases in 18 months | Ahmed: Indian M. Gaz.[125] |
| India, 1939 | Describes 5 cases; 12 cases seen at the medical school yearly | Sen Gupta, Rai Chaudhuri, Chaudhuri and Napier [125] |
| India, 1942 | | Ahmed: J. Indian M. A.;[125] present in upper provinces |
| India, 1940 | 20 cases | Goodall;[125] in India cases of pellagra are frequently met |
| India, 1939 | "Frequent" | Napier [125] thinks pellagra is frequent in India but is not diagnosed |
| Straits Settlements and Malaya, 1937 | 64 cases in 10 years with 1 death | Ann. Rep. M. Dept. Straits Settlements, Fed. Malay States and Unfed. Malay States, 1938 |
| Malaya, 1935 | 3 cases | Landor, J. V., and Pallister, R. A.: Tr. Roy. Soc. Trop. Med. & Hyg. **29**: 121, 1935; disease sporadic in Malaya |
| Straits Settlements, 1932 | 2 cases | Stannus,[119] quoting reports of medical departments of British colonies |
| Hong Kong, 1932 | 24 cases | |
| Trinidad, 1933 | 1 case | |
| St. Christophers, 1932 | 1 case | |
| Antigua, 1933 | 2 cases | |
| British Honduras, 1932 | 1 case | |
| Bahamas, 1928-1932 | 404 cases | |
| Russian Turkestan, 1934 | 20 cases at Tashkent | Wyjasnowsky [126] |
| China, 1934 | 30 cases | Yang and Huang;[127] occurred in army camp |
| Manchuria, 1934 | 3 cases | Yu [127] |
| Korea, 1926 | Present in leprosy colonies | Wilson [127] |
| Japan, 1925 | 72 cases reported in Japan to 1925 | Itoh [128] |
| China, 1941 | 40 cases | Morris, Hwang and Kuo;[127] all from 1 war refugee camp |
| Korea, 1939 | 39 cases | Urabe [127] |

debility, progressive anemia, a hemorrhagic tendency and skeletal changes of infants and children as the result of arrestment of bone development and hemorrhage.

The disease is of worldwide occurrence. Case studies and group surveys have been reported from Africa,[138] China,[139] Australia[140] and its territories,[141] Malaya,[142] the Philippines,[143] Czechoslovakia,[144] France,[145] Norway,[146] Rumania,[147] Spain,[148] Switzerland,[149] the Faroe Islands,[150] Greenland,[151] the United States[152] and of 10,000 natives studied had clinical evidence of scurvy. The crowded housing, increased incidence of infectious diseases, chronic fatigue and native customs of preparation of food were attributed as causative factors. In several studies where the incidence reported has been based on the demonstration of low blood vitamin C levels, in selected groups, the prevalence of hypo-vitamin C appears alarming. During the winter of 1937-1938 among school children studied in Lau-

TABLE 7.—*Incidence of Riboflavin Deficiency*

| Area and Year | Incidence | References and Comment |
|---|---|---|
| Georgia, 1939 | 3 cases | The Odens and Sebrell;[150] all had cheilosis |
| New York, 1939 | 15 cases | Jolliffe, W.; Fern, H. D., and Rosenblum, L. A.: New England J. Med. **221**: 24, 1939; all had cheilosis |
| Georgia, 1939 | 6 cases | Sydenstricker, V. P.; Geeslin, L. E.; Templeton, C. M., and Weaver, J. W.: J. A. M. A. **113**: 1697, 1939; all had cheilosis |
| Alabama, 1939 | 977 cases of multiple B vitamin deficiency | Spies, T. D.; Vilter, R. W., and Ashe, W. F.: J. A. M. A. **113**: 931, 1939 |
| Alabama, 1940 | 241 cases in infants and children | Spies, Bean, Vilter and Huff[131] believe ariboflavinosis to be the most common clinical deficiency disease |
| Georgia, 1940 | 45 cases | Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M., and Kruse, H. D.: J. A. M. A. **114**: 2437, 1940; patients had eye lesions responding to riboflavin therapy |
| Georgia, 1940 | 9 cases | Kruse, H. D.; Sydenstricker, V. P.; Sebrell, W. H., and Cleckley, H. M.: Pub. Health Rep. **55**: 157, 1940; eye lesions |
| New York City, 1941 | Mild deficiency in 4.7% of 350 well-to-do children; mild deficiency in 75.8% of 495 pupils from low income groups; mild deficiency in 34.4% of 143 WPA employees | Wiehl and Kruse;[6] diagnoses made purely on the basis of eye examination |
| New Orleans, 1942 | 68 of 200 individuals admitted consecutively to medical wards of Charity Hospital had some evidence of riboflavin deficiency | Goldsmith[132] finds ariboflavinosis to be the most common deficiency |
| India, 1936 | 41 cases of "angular stomatitis" | Aykroyd and Kishman[134] |
| India, 1942 | 13 cases | Aykroyd and Verma;[134] "superficial keratitis" |
| India, 1942 | 50 cases | Verma;[134] "superficial keratitis" |
| Malaya, 1931 | Prevalent in prisons at Singapore and Johore | Landor and Pallister;[136] syndrome characterized by cheilosis, glossitis, scrotal dermatitis and combined degeneration of the spinal cord |
| China, 1941 | 47.9% of 186 refugees had riboflavin deficiency | Hou[135] |
| Africa, Gold Coast, 1942 | 6 cases | Pursell;[137] cases chiefly glossitis |
| Africa, Belgian Congo, 1940 | Many types of glossitis and angular stomatitis are seen among the natives of the Belgian Congo | Barlovatz[137] |
| England, 1942 | 3 cases | Scarborough;[133] 3 cases of keratitis responding to riboflavin deficiency |

TABLE 8.—*Reports of Vitamin C Deficiency*

| Country and Year | Incidence of Scurvy Reported | Comment | References |
|---|---|---|---|
| Rhodesia, South Africa, 1932 | 80% | 10,000 native mine employees | Dry[154] |
| Lausanne, France, 1938 | 90% | Survey of school children during winter months by blood vitamin C determinations; attributed to drop in milk and potato content of diet | Messerli and Heimann[155] |
| Bucharest, Rumania, 1941 | 90% | Survey among school children during winter months by blood studies; incidence due to inadequate winter diet | Mezincesco[147] |
| Nashville, Tenn., 1940 | 50% | Study of 500 children attending pediatric clinic by blood analysis technic | Milam[156] |
| Chaco area, Uruguay, 1939 | 3.4 to 15.5% | Observed incidence among hospital patients of military and civilian sources respectively | Quiroz[153] |
| Switzerland, 1940 | 57% | 94 soldiers studied by blood analysis | Gander and others[157] |
| Switzerland, 1942 | 38% | 100 civilians of all social and age groups employed in antiaircraft corps | Barrelet[158] |
| Prague, Czechoslovakia, 1939 | 10% | 180 school children studied by blood assay | Bytch[159] |
| New York City, 1941 | 6.7% | A selected group as determined by blood analysis | Wiehl and Kruse[6] |
| South Carolina, 1942 | 1.5% | 400 citizens of small mill village as determined by blood studies | Croft and Snorf[160] |
| England, 1942 | Not significant | Selected groups of school children and medical students as studied by blood assay | Francis and Wormall;[161] Harris[161] |

South America.[153] The endemic or epidemic proportions of the disease depend on many factors. In 1932 a report from Rhodesia[154] revealed that 80 per cent sanne, France,[155] 90 per cent had low blood levels. A group of school children studied during the winter of 1941 in Bucharest, Rumania,[147] revealed low blood levels in 90 per cent. The authors independently attribute this high incidence to the inadequacy of the

138. Hofmeyr, H. O.: Proc. Staff Meet., Mayo Clin. **16**: 644 (Oct. 8) 1941. Henson, J.: South African M. J. **12**: 918 (Dec. 24) 1938; Ann. Rep. M. Services, Nigeria, 1936-1937. Drogoz & Henric: Ann. Med. Pharm., Colon **35**: 1093, 1937. Dry.[154]

139. Morgan, Julia, and Gault, A. S.: Chinese M. J. **60**: 141 (Aug.) 1941.

140. Health (Australia) **15**: 15, 140 (Nov.) 1937.

141. Army M. Bull. No. 65, 1943, p. 32.

142. Ann. Rep. M. Dept., Straits Settlements, 1929-1935.

143. League of Nations, Health Organization, Intergovernmental Conference on Nutrition, Geneva, 1937.

144. Charvat, J.: Bull. Office internat. d'hyg. pub. **30**: 591 (March) 1938. Bytch.[159]

145. Ann. Rep. Internat. Health Div. Rockefeller Foundation, 1941, p. 142. Messerli and Heimann.[155]

146. Langfeldt, E.: Nord. med. tidskr. **15**: 244, 1938.

147. Mezincesco, M. D.: Ztschr. f. Vitaminforsch. **11**: 376, 1941.

148. Robinson, W. D.; Janney, J. H., and Grande Covian, Francisca: J. Nutrition **24**: 557 (June) 1942.

149. Gander and others.[157] Barrelet.[158]

150. Wagner, K. H.: Deutsche med. Wchnschr. **67**: 1232, 1941.

151. Bøje, O.: Nord. Med. **1**: 740-743, 1939; abstr. Chem. Zentralbl. **8**: 1224, 1941.

152. Minot, A. S.; Dodd, Katharine; Keller, Margaret, and Frank, Helen: J. Pediat. **16**: 717 (June) 1940. Overstreet, R. M.: Northwest. Med. **37**: 175 (June) 1938. Wiehl and Kruse.[6]

153. Quiroz, J. D: Bull. de la Oficina Saniteria Panamericanos **78**: 55, 1939.

154. Dry, T. J.: Proc. Staff Meet., Mayo Clin. **7**: 309 (May 25) 1932.

155. Messerli, F. M., and Heimann, F.: Rev. d'hyg. **60**: 20 (Jan.) 1938.

winter diet to furnish vitamin C. Among 500 children seen in a pediatric clinic in Tennessee in 1940, 50 per cent had low blood levels for vitamin C.[156] A study among hospital cases in Uruguay[153] in 1939 revealed an incidence of 15.5 per cent among the civilian population and 3.4 per cent among the soldiers. In 1940 among a group of 94 Swiss soldiers[157] whose enlistment period was in excess of nine months, 57 per cent had blood determinations at deficiency levels, while among a group of 100 civilians[158] studied in 1942, 38 per cent demonstrated low blood levels.

Less alarming figures have been reported from similar surveys, utilizing blood level determination, among selected groups. In Prague,[159] in 1939, 10 per cent of 180 school children between the ages of 12 and 20 years had low blood levels. In New York City,[6] in 1941, 6.7 per cent of a selected group were deficient. In South Carolina,[160] in 1942, 1.5 per cent of 400 people

TABLE 9.—*Occurrence of Vitamin K Deficiency*

| Area, Year | Condition | Incidence or Number of Cases | Comment | References |
|---|---|---|---|---|
| United States 1941 | Hemorrhagic disease of newborn | Untreated, 11 of 25; K to mother during labor, 10 of 53; K to mother before labor, 3 of 23 | ..... | Pray, L. G.; McKeown, H. S., and Pollard, W. E.: Am. J. Obst. & Gynec. **42**: 836, 1941 |
| United States 1941 | Retinal hemorrhage | Untreated, 56 of 223, K to mother during labor, 34 of 223; K to mother before labor, 2 of 50 | ..... | Maumenee, Hellman and Shettles [161b] |
| United States 1941 | Hemorrhagic disease of newborn | Untreated, expectancy 5 cases; treated, 0 of 556 | ..... | Javert, C. T., and Macri, C.: Am. J. Obst. & Gynec. **42**: 415, 1941 |
| United States 1940 | Death from hemorrhagic disease of newborn | Untreated, 2.3%; treated, 0.25% | Deaths (total) 4.1% and 1.5% respectively | Hellman, L. M.; Shettles, L. B., and Eastman, N. J.: Am. J. Obst. & Gynec. **40**: 844, 1940 |
| United States 1940 | Hemorrhage or birth injury | Untreated, 23 of 219; treated, 4 of 400 | ..... | Waddell and Lawson [161a] |
| | Prothrombin deficiency | 111 of 189 | | |
| United States 1940 | Hemorrhagic disease of newborn | 22 cases | Responded to K | Poncher, H. G., and Kato, Katsuji: J. A. M. A. **115**: 14, 1940 |
| United States 1939 | Hemorrhagic disease of newborn | 7 cases | Responded to K | Waddell, W. W., Jr., and Guerry, DuPont: J. Pediat. **15**: 802, 1939 |
| United States 1939 | Hemorrhagic disease of newborn | 1 case | Decreased clotting time in 10 of 10 | Waddell, W. W., Jr., and Guerry, DuPont: J. A. M. A. **112**: 2259, 1939 |
| United States 1940 | Hypoprothrombinemia | 41 cases | Treated successfully; 8 with liver damage did not respond | Andrus, P. M., and Lord, J. W., Jr.: Ann. Surg. **112**: 783, 1940 |
| United States 1940 | Hypoprothrombinemia | 39 cases | Treated successfully; 6 with liver damage did not respond | Weir, J. F.; Butt, H. R., and Snell, A. M.: Am. J. Digest. Dis. **7**: 485, 1940 |
| United States 1940 | Hypoprothrombinemia | 20 cases | All except those with liver damage treated successfully; 7 with hemorrhagic bleeding stopped | Norcross, J. W., and McFarland, M. D.: J. A. M. A. **115**: 2156, 1940 |
| United States 1940 | Hypoprothrombinemia | 28 cases | Treated successfully: 18 did not respond many of these had liver damage | Pohle, F. J., and Stewart, J. K.: J. Clin. Investigation **19**: 365, 1940 |
| United States 1940 | Hypoprothrombinemia | 17 cases | Treated successfully; 3 with liver damage did not respond | Butt, H. R.; Snell, A. M.; Osterberg, A. E., and Bollman, J. L.: Proc. Staff Meet., Mayo Clin. **15**: 69, 1940 |
| United States 1940 | Hypoprothrombinemia | 10 cases | 9 responded; 3 of these had bleeding which stopped | Rhoads, J. E., and Fliegelman, M. T.: J. A. M. A. **114**: 400, 1940 |
| United States 1939 | Hypoprothrombinemia in obstructive jaundice | 5 cases | Responded to K | Stewart, J. D., and Rourke, G. M.: New England J. Med. **221**: 403, 1939 |
| United States 1939 | Hypoprothrombinemia in obstructive jaundice | 12 cases | Responded to K | Stewart, J. D.: Ann. Surg. **109**: 588, 1939 |
| | Hemorrhage after operation | 4 cases | Responded to K | |
| United States 1940 | Bleeding in obstructive jaundice | 11 cases | Responded to K; 5 patients with liver damage did not respond | Aggeler, P. M.; Lucia, S. P., and Goldman, L.: Proc. Soc. Exper. Biol. & Med. **43**: 689, 1940 |
| Scotland 1940 | Intercranial hemorrhage | 1 to 2% | 85% die in first 3 days; 25% of survivors have motor or mental involvement | Macpherson, A. I. S.; McCallum, E., and Haultain, W. F. T.: Brit. M. J. **1**: 839, 1940 |
| | Hypoprothrombinemia | 67 cases | K raised above danger point (to 36 babies and to 31 mothers during or before labor) | |
| Scotland 1939 | Hemorrhagic tendency with jaundice | 4 cases | Responded to K | Illingsworth, C. F. W.: Lancet **1**: 1031, 1939 |
| Denmark 1941 | Hemorrhagic disease of newborn | 65 cases | Responded to K | Dam, H., and Plum, P.: Monatsschr. f. Kinderh. **87**: 55, 1941 |
| Denmark 1940 | Hemorrhagic disease of newborn | 31 cases | Responded to K | Plum, P., and Dam, H.: Ugesk. f. læger, **102**: 1029, 1940 |
| Denmark 1939 | Hemorrhagic disease of newborn | 4 cases | 2 responded to K | Dam, H.; Tage-Hansen, E., and Plum, P.: Ugesk. f. læger **101**: 896, 1939 |
| Sweden 1940 | Bleeding in obstructive jaundice | 4 cases | Responded to K | Hedenstedt, S.: Nord. Med. **6**: 789, 1940 |
| Canada 1940 | Bleeding in obstructive jaundice | 17 cases | Responded to K | Townsend, S. R., and Mills, E. S.: Canad. M. A. J. **43**: 541, 1940 |
| Canada 1939 | Bleeding in obstructive jaundice | 10 cases | 9 responded to K | Townsend, S. R., and Mills, E. S.: Canad. M. A. J. **41**: 111, 1939 |
| Germany 1939 | Bleeding in obstructive jaundice | 1 case | Responded to K | Koller, F., and Wahrmann, F.: Klin. Wchnschr. **18**: 1058, 1939 |

156. Milam, D. F.: Am. J. Pub. Health **32**: 406 (April) 1942.
157. Gander and others: Ztschr. f. Vitamin. **11**: 121-128, 1941.
158. Barrelet, P.: Schweiz. med. Wchnschr. **72**: 796 (July 18) 1942.
159. Bytch, L.: Rev. franç. de pediat. **15**: 188, 1939.

studied in a mill village were also demonstrated to have low blood vitamin C levels. In England,[161] comparative studies done in 1939 and 1942 among selected school children and medical students revealed "no significant incidence of scurvy" and no increase in the occurrence rate since the onset of World War II, although the determined blood levels were on the average lower for the latter study period.

## VITAMIN K

Vitamin K deficiency manifests itself as a tendency to hemorrhage, brought about by a lowered prothrombin level of the blood. It is believed that the normal human adult can dispense with this vitamin in the diet because of synthesis by bacteria in the intestine. It follows and is supported by clinical findings that K avitaminoses will be found only in the newborn before the bacterial flora has become established and in adults when there is interference with fat absorption.

A tendency to hemorrhage is not a proof of vitamin K deficiency, but it has become well established that this vitamin is of value in preventing hemorrhagic disease of the newborn and the bleeding of obstructive jaundice and a number of other conditions.

Most cases of hypoprothrombinemia except those which are due to liver damage have been found to respond to vitamin K.

TABLE 10.—*Nutritional Anemia*

| Location and Date | Number of Persons Studied | Age | Sex | Mean Hemoglobin: Per Cent of Entire Group | Mean Hemoglobin: Hemoglobin | Mean R. B. C.: Per Cent of Entire Group | Mean R. B. C.: R. B. C., Millions | Per Cent Deficient | Standard Hemoglobin | References |
|---|---|---|---|---|---|---|---|---|---|---|
| Rural Pennsylvania and small Pennsylvania city 1939 | 898 | All | ♂ and ♀ | ..... | ..... | 41.24<br>19.02<br>19.87<br>11.11<br>8.76 | 4.76 or +<br>4.75-4.51<br>4.50-4.26<br>4.25-4.01<br>4.00 or — | ..... | ..... | Mack, P. B.; Smith, J. M.; Logan, C. H.; Stewart, A. H., and Dodds, Paul: Richards Institute Pub. 2, part I, December 1942 |
| Pennsylvania metropolitan school 1939 | 1,362 | School age | 709 ♀<br>653 ♂ | 23.03<br>46.05<br>29.44<br>1.03<br>0.00 | 13.0 Gm.+<br>12.99-11.50<br>11.49-10.00<br>9.99- 8.50<br>8.49 or — | 47.07<br>43.49<br>17.03<br>9.03<br>3.38 | 4.76 or +<br>4.75-4.51<br>4.50-4.26<br>4.25-4.01<br>4.00 or — | ..... | ..... | |
| Pennsylvania 1939 | 2,400 | Preschool | ♂ and ♀ | ..... | ..... | ..... | ..... | 51 ♂<br>56 ♀ | >11.5 Gm. | Mack, P. B.; Smith, J. M.; Logan, C. H., and O'Brien, A. T.: Milbank Quart. **19**, No. 3, 1941 |
| | | School | ..... | ..... | ..... | ..... | ..... | 19 ♂<br>30 ♀ | 10-11.5 Gm. | |
| | | Adult | ..... | ..... | ..... | ..... | ..... | ±35 ♂<br>±50 ♀ | 10-11.5 Gm. | |
| North Carolina town of 400 1940 | ? | Adult<br>Children | .....<br>..... | 100%<br>100% | 13.7 ♂, 12.6 ♀<br>12.3 ♂, 12.6 ♀ | ..... | ..... | ..... | ..... | Milam [156] |
| Oklahoma City 1939 | 1,000 pregnant women last trimester | Adult | ♀ | 38.0<br>39.1<br>22.2<br>0.7 | 10.2-11.9<br>11.9-13.6<br>13.6-15.3<br>15.3+ | 16.4<br>4.71<br>29.2<br>4.6<br>2.7 | 3.0-3.5<br>3.5-4.0<br>4.0-4.5<br>4.5-5.0<br>5.0+ | ..... | ..... | Eskridge, J. B., and Serwer, M. J.: South. Med. J. **32**: 24, 1939 |
| Gainesville, Fla. 1939 | 620 | School age | ♂ and ♀ | 2.0<br>12.2<br>28.5<br>28.2<br>15.6<br>13.5 | 91-100%<br>81- 90%<br>71- 80%<br>61- 70%<br>51- 60%<br>21- 50% | ..... | ..... | ..... | 13.7 Gm. or 100% *<br>9.6 Gm. or 70% †<br>11.7 Gm. or 85% ‡ | Abbott, O. D., and Ahman, C. F.: Am. J. Dis. Child. **58**: 811, 1939 |
| | 263 | Preschool | ♂ and ♀ | 3.4<br>23.1<br>40.0<br>14.4<br>7.2<br>4.8 | 91-100%<br>81- 90%<br>71- 80%<br>61- 70%<br>51- 60%<br>21- 50% | | | ..... | 13.7 Gm. or 100% *<br>9.6 Gm. or 70% †<br>11.7 Gm. or 85% ‡ | |
| New York City 1941 | 175<br>161<br>241<br>184 | High school<br>High income<br>Low income<br>..... | ♂<br>♀<br>♂<br>♀ | .....<br>.....<br>.....<br>..... | .....<br>.....<br>.....<br>..... | .....<br>.....<br>.....<br>..... | .....<br>.....<br>.....<br>..... | 0<br>3.1<br>2.5<br>4.3 | ..... | Wiehl and Kruse [6] |
| New York State 1940 | 100 | Adults | ♂ and ♀ | ..... | ..... | ..... | ..... | 23 | 10.2 Gm. per 100 cc. | Scott, J. R., and Janeway, M. M.: New York State J. Med. **40**: 440, 1940 |
| New York City 1940 | ... | Adults | ♂<br>♀ | .....<br>..... | .....<br>..... | .....<br>..... | .....<br>..... | 7.6<br>6.8 | ♂ 14 Gm.<br>♀ 12 Gm. | N. R. C. Series No. 110, April 1942 |
| Madrid, Spain 1941 | 561 | All ages | ♂<br>♂♀<br>♂♀<br>♀ | .....<br>.....<br>.....<br>..... | .....<br>.....<br>.....<br>..... | .....<br>.....<br>.....<br>..... | .....<br>.....<br>.....<br>..... | 16<br>18<br>31<br>33 | 12 Gm. per 100 cc.§ | Robinson, W. D.; Janney, J. H., and Grande (Covian) Francisco: J. Nutrition **24**: 557, 1942 |
| Scotland 1933 | ? | Children<br>Adolescent<br>Adult | ♂ and ♀<br>♀<br>♀ | .....<br>.....<br>..... | .....<br>.....<br>..... | .....<br>.....<br>..... | .....<br>.....<br>..... | 32<br>16<br>45 | ..... | Davidson, L. S. P.; Fullerton, H. W.; Howie, J. W.; Croll, J. M.; Orr, J. B., and Godden, W.: Brit. M. J. **1**: 685, 1933 |
| Boston 1939 | ? | Adult | ♀ | ..... | ..... | ..... | ..... | 16 | ..... | Heath, C. W.: Symposium on the Blood and Blood Forming Organs, Wisconsin Press, 1939 |
| Michigan 1939 | 158 | Adult (pregnant) | ♀ | ..... | ..... | ..... | ..... | 26.6 | 10 Gm. per 100 cc. | Bethall, F. H.; Gardner, S. H., and MacKinnon, Frances: Ann. Int. Med. **13**: 91, 1939 |
| New York City 1939 | 325 | Adult (pregnant) | ♀ | ..... | ..... | ..... | ..... | 72 | 11.6 Gm. per 100 cc. | Labate, J. S.: Am. J. Obst. & Gynec. **38**: 48, 1939 |
| Kentucky 1940 | ? | Adult (pregnant) | ♀ | ..... | ..... | ..... | ..... | 30 to 60 | ..... | Gordon, Harold: Kentucky M. J. **38**: 415, 1940 |

* Normal. † Anemic. ‡ Subnormal. § Standard red blood cells, 4,120,000.

In summary it would appear that vitamin C deficiency is of worldwide occurrence in significant numbers of people. Although low blood levels of vitamin C may and do occur without evident manifestations of scurvy, this finding indicates at least an intake of vitamin C below that necessary to maintain the individual's body reserves at the highest level.

160. Croft, J. D., and Snorf, L. D.: Am. J. M. Sc. **198**: 403 (Sept.) 1939.

161. Francis, G. E. C. and Wormall, A.: Lancet **1**: 647 (May 30) 1942. Harris, L. J., ibid. **1**: 642 (May 30) 1942.

Avitaminosis K appears to have been studied most extensively in the United States, in Denmark and in the British Isles. Very little information is available from other sections of the world. By far the highest incidence is in the newborn; other cases are negligible in comparison. Estimates of prothrombin deficiency in very young infants range as high as 60 per cent,[161a] and an incidence of retinal hemorrhage as high as 25 per cent has been observed.[161b]

### NUTRITIONAL ANEMIA

The term "nutritional anemia" is restricted to the anemia resulting from insufficient dietary intake of iron. Anemias indirectly arising from other nutritional deficiency such as that which accompanies scurvy, pellagra or hypoproteinemia are not included here.

Nutritional anemia cannot be regarded as a clearly defined clinical entity. Standards of optimal hemoglobin concentration and optimal red blood cell count for persons of each age, sex or race are not generally agreed on.[6] Moreover, certain normal physiologic functions such as pregnancy, pubescence, catamenia and the menopause materially alter the blood picture in so complex a manner that the definition of the norm for these special states is uncertain.[162] The situation is further complicated by the fact that other causes of anemia such as chronic latent blood loss, local infection or tuberculosis may be readily overlooked in large scale investigations.

The clinical features of nutritional anemia are likewise not very clearcut. The dietary history affords the most pertinent positive information. In evaluating the dietary history, local variations in the iron content of foods must be kept in mind. The symptoms are somewhat generalized and include lack of energy, headache, vertigo, dyspnea and palpitations. In children, behavior difficulties such as failure to concentrate and physical indolence are observed. The condition is commonly accompanied by no distinct symptoms whatever.

Physical findings include pallor, loss of skin turgor, suboptimal weight and reduced muscle tone. In advanced cases a soft apical systolic murmur may be heard and the pulse is rapid and of poor quality.[163]

Most often, however, the diagnosis rests solely on laboratory findings. Reznikoff states that, "hematologically, the striking features of iron deficiency from any cause are the relatively marked decrease of hemoglobin compared to the red blood cell reduction and the small size of the cells, giving a low volume index, usually less than 0.75." [164]

Recent studies have been concerned both with the development of adequate diagnostic standards and with the determination of the prevalence and distribution of the deficiency. Despite numerous fairly elaborate studies, only a beginning has been made. In table 10 there have been summarized those studies of the past decade which afford epidemiologic data concerning nutritional anemia. The groups studied vary widely and include preschool children, school children, pregnant women and general populations. Standards for the determination of deficiency are frequently not stated and the stated standards vary widely from survey to survey. Moreover, the inherent error in the several laboratory procedures employed in the respective surveys is not at all comparable, although in all instances it is admittedly great. For these reasons each of the recorded studies must be regarded as a distinct source of information bearing on the special group, and no general statistical summary is warranted.

Disregarding these limitations, we may observe from isolated studies that at least in certain communities nutritional anemia should be given close consideration. Thus, about 50 per cent of 2,400 children studied in Pennsylvania in 1939 were anemic. In Michigan 26.6 per cent of 158 pregnant women were found anemic, and in Boston 16 per cent of adults studied were anemic. In New York City 72 per cent of 325 pregnant women were anemic. In Florida in 1939 more than 50 per cent of 620 school children were found to have subnormal hemoglobin. In Scotland, in 1939, 32 per cent of children and 45 per cent of adults examined were anemic, and in Madrid, Spain, in 1941, 16 to 18 per cent of 561 persons had low hemoglobin (table 10).

Accordingly, Jolliffe, McLester and Sherman [162] state that combining such data indicates "anemia in from 1.5 to 85 per cent of children, 3.6 to 30 per cent of adults and 9 to 72 per cent in pregnancy." Obviously the wide range of these estimates indicates that they are not particularly informative of the actual occurrence of nutritional anemia in the world population.

Such diverse and yet limited information affords too spotty a view of the character and scope of the problem of nutritional anemia to constitute a basis for sound public health practice. Nevertheless it is clear that where the condition has been searched for many cases have been found. In all probability nutritional anemia is of widespread, worldwide occurrence, and further extensive observations should be carried out in order to set up suitable public health and dietaary practices to prevent this condition.

### THE PROBLEM OF ADEQUATE NUTRITION

International attention was first given to nutrition and health by the League of Nations beginning in 1925 and culminating in the reports of the Technical Commission on Nutrition [165] and the Mixed Committee on Nutrition in 1937.[166] It is obvious that as measured by any modern standard of adequate nutrition much of the world's population is subsisting on inadequate food. In terms of adequate food for every one, no food surplus has ever existed. In terms of dietary adequacy the world has never had enough to eat. So-called overproduction and apparent surpluses have in reality been failures to secure adequate distribution. The recent United Nations Conference on Food and Agriculture [167] recognized that national and international agricultural policies must be directed toward obtaining a food supply adequate for health.

Although poverty is the principal cause of malnutrition, general economic improvement will not give every one an adequate diet. Faulty food distribution is the

161a. Waddell, W. W., Jr., and Lawson, G. M.: Hemorrhagic Diathesis of the Newborn, J. A. M. A. **115**: 1416 (Oct. 26) 1940.

161b. Maumenee, A. E.; Hellman, L. M., and Shettles, L. B.: Factors Influencing Plasma Prothrombin in the Newborn Infant, Bull. Johns Hopkins Hosp. **68**: 158 (Feb.) 1941.

162. Jolliffe, Norman; McLester, J. S., and Sherman, H. C.: The Prevalence of Malnutrition, J. A. M. A. **118**: 944 (March 21) 1942.

163. Osler's Textbook of Medicine, ed. 14, H. S. Christian, editor, New York, D. Appleton & Co., 1942.

164. Cecil, R. L.: A Textbook of Medicine, ed. 5, Philadelphia, W. B. Saunders Company, 1942, p. 1071.

165. Physiological Bases of Nutrition, League of Nations Publications: II. Economic and Financial, 1936, II, B 4.

166. Interim Report of the Mixed Committee on the Problem of Nutrition, League of Nations Publications: II. Economic and Financial, 1936, II, B 3.

167. United Nations Conference on Food and Agriculture: Final Act and Section Reports, Dept. of State Publication 1948, Conference Series 52, 1943. Parran, Thomas: A Blueprint for the Conquest of Hunger, Pub. Health Rep. **58**: 893 (June 11) 1943. Editorial, Am. J. Pub. Health. **33**: 847, 1943.

most important contributory factor, and ignorance of the rules of good diet plus indifference to the consequences and bad dietary habits are the contributory underlying causes.

Great Britain has shown that a national food policy based on nutritional adequacy can control malnutrition. Close control of food production, importation and prices together with strict rationing and with a food distribution system planned with the assistance of nutrition experts with the goal of adequacy instead of profit has assured an individual availability of foods with the result that, in spite of poorer living conditions incident to the war, the infant mortality in 1942 was the lowest on record and health has been maintained at a high level with a decreased general death rate and a negligible incidence of deficiency diseases.

From the point of view of preventive medicine the problem of adequate nutrition is so different from other health problems that it requires a new approach. Its ramifications extend far into our whole economic structure. Such diverse problems as the control of crop production, farm machinery, manpower, food distribution, transportation, food preservation and processing, storage and food preparation as well as nutrition education and the diagnosis, prevention and treatment of deficiency diseases are all involved. It is obvious that problems of this range and magnitude cannot be solved by physicians, health officers or any other one agency alone. The first essential is close cooperation and intimate relations among a number of agencies, including physicians and health officers.

A number of official and voluntary agencies in this country have been working on certain aspects of our nutrition problem for many years with little participation by physicians except from some health officers. The home economics and agriculture teachers in our high schools and colleges, the Agricultural Extension Service, the American Red Cross, the Children's Bureau of the Department of Labor and numerous other organizations have had continuing programs for a long time.

Many of our state health departments have established and maintained a small nutrition service at the state level with the assistance of the Children's Bureau. The attention here during peacetime was focused primarily on problems of maternal and child health, and an excellent start has been made. However, there are other population groups which also may be regarded as especially vulnerable from a nutritional point of view and to whom it is essential that attention also be given especially in wartime, for example school children, adolescents and workers in essential industries. In order to deal more effectively with these varied problems the regular nutrition activities of various government and voluntary agencies have been intensified, expanded and coordinated. A first meeting of representatives of these agencies was held in 1940, and in May 1941 President Roosevelt called the First National Nutritional Conference in Washington.[168]

The National Nutrition Program was based on the recommendations of this conference, and coordination was obtained through the Nutrition Division of the Office of Defense Health and Welfare Services. These activities have now been incorporated into the Nutrition and Food Conservation Branch of the War Food Administration.

Regional nutritionists carry out the functions of this branch from the Food Distribution Administrative regional offices. On invitation these nutritionists work with state and local nutrition committees in planning and developing nutrition programs and projects. The most important accomplishment of this office has been the successful coordination of the nutrition program of various agencies, recognizing the place of each but centering attention on the common objective. It has shown that a coordinated program of this magnitude can be made to work in this country.

Nutrition committees have been formed in every state and in Hawaii and also are working on local nutrition problems in many counties, cities and local communities. In many instances there has been little or no participation by physicians or health officers in spite of invitations to medical societies and health departments to send representatives. The work of these committees has consisted mainly in the organization of nutrition classes, preparation and distribution of educational material, food demonstrations, victory gardens and home food preservation, and it is expected that they will play an increasingly important role in war food programs through school lunch activities and nutrition in industry subcommittees. If properly developed they should become the local body through which all the food and nutrition problems of the community are attacked.

The ultimate purpose of a civilian wartime food program is to assure "enough to eat" to every one, so that the war may be fought with the utmost efficiency. The phrase "enough to eat" in its proper use must mean not only enough in quantity but also enough of all essential dietary elements. This means that the entire program must be planned on a sound technical nutritional basis with adequate control of distribution together with price control of those constituents of the nation's food supply necessary to secure dietary adequacy.

Failure to recognize the necessity for basing the control on nutritional adequacy, or half-way measures of control, defeat the whole purpose of the program and are worse than no control in that they create a false sense of dietary security, and a ration coupon becomes a symbol of unobtainable food rather than a guaranty of a fair share of an item necessary for the maintenance of health.

It is also essential that any such program take into account the greater physiologic needs of the "vulnerable groups" in the population, among the most important of these groups during war being the workers in war industries. Differential rationing by allotting more ration coupons to such groups would threaten the whole rationing structure because of difficulties in administration and the great difficulty in assessing the actual needs of the individual based on his special requirements. In general the most practicable solution is to develop feeding facilities within each industrial plant which can supply an adequate midshift meal to every employee without requiring ration coupons. In a few industries operating under special conditions of isolation from the usual food supply, it may be necessary to supply extra food to the entire establishment. Here the allocation is made to the group and not to the individual. Rare exceptions, such as sheep herders, may require special allocations.

168. Proceedings of the National Nutrition Conference for Defense, U. S. Govt. Printing Office, 1942.

The aspect of industrial nutrition which involves the community can be attacked by the local nutrition committee. Inplant feeding should be regarded as one aspect of a properly developed industrial hygiene program. It should be approached through the plant medical officer or safety director after the plant management has agreed to the program.

At the federal level the War Food Administration works closely with the Industrial Hygiene Division of the National Institute of Health of the United States Public Health Service. At the state level, when state health departments have industrial hygiene officers they should be one of the points of contact with the plant, using the advice and assistance of the local and state nutrition committee. Because of the scope and importance of the industrial nutrition problem the War Food Administration has appointed regional nutrition representatives to work with state and local committees as well as health officers and plant officials.

On request from industrial plants, industrial nutritionists assist in planning employee feeding and nutrition education programs and in handling applications for essential equipment and food. They also work with labor groups in promoting better eating habits.

TABLE 11.—*Necessary Foods*

1. Green and yellow vegetables, some raw, some cooked, frozen or canned.
2. Oranges, tomatoes, grapefruit or raw cabbage or salad greens.
3. Potatoes and other vegetables and fruits raw, dried, cooked, frozen or canned.
4. Milk and milk products, fluid, evaporated, dried milk or cheese.
5. Meat, poultry, fish or eggs or dried beans, peas, nuts or peanut butter.
6. Bread, flour and cereals, whole grain or enriched or restored.
7. Butter and fortified margarine (with added vitamin A). "Eat some food from each group every day."

"In addition to the basic 7, eat any other foods you want."

Further instructions in order to cover possible wartime shortages are as follows:

| *If scarce in* | *Use more from* |
|---|---|
| Group 2 | Group 1, 3 |
| Group 4 | Group 1, 5, 6 |
| Group 5 (meats) | Group 4, 5 (eggs) |
| Group 7 | Group 1, 4 |

In many states industrial nutrition subcommittees have been organized under the state nutrition committee. The representative of the health department should work with these subcommittees, which include industrial physicians, caterers, representatives of labor, plant management and other interested groups.

Nutrition committees throughout the country are constantly striving to improve the public knowledge of nutrition and to develop better food habits. Food shortages make these activities more important than ever. This education is based on food groups designed to yield nutritional adequacy with considerable latitude in the choice of food items. The recommendation is a type diet which for application requires local adaptation to specific items. The necessary foods are listed in seven groups (table 11).

Physicians and health officers should assist in the promotion of sound nutrition education as well as in promoting good food programs designed to improve nutrition. The health officer has both an opportunity and an obligation here in preventive medicine which cannot be performed as well by any other group. The concept of the prevention of disease must be enlarged to include an effort to attain the best possible level of health which is unknown in the absence of good nutrition.

The fact that malnutrition and deficiency diseases usually appear insignificant in mortality and morbidity tables does not reflect the real importance of nutrition in our national health. Although good nutrition does not guarantee good health, poor nutrition can and often does contribute to mortality from other primary causes, while optimum nutrition can contribute to optimum health.

The health officer and physician can help determine the prevalence of malnutrition and relate nutrition problems to other public health and medical problems. Some of the more important activities for health departments in developing this field in collaborating with existing programs were recently proposed by Sebrell and Wilkins [169] as follows:

STATE HEALTH DEPARTMENT ACTIVITIES

1. Collect information and do appraisals on the incidence and types of deficiency diseases and on food habits in geographical areas and population groups, especially children, pregnant and lactating women and industrial workers. Even small samplings are of value in pointing the way to more comprehensive appraisals.

2. Offer assistance in the diagnosis of nutritional deficiencies. Here is a health department service which is in line with sound public health principles and which will strengthen the work of other agencies in this field. At the same time the efforts of other agencies will contribute greatly to creating a demand for this type of service.

3. Prepare and distribute simple attractive literature dealing with state nutrition problems. Such literature should be prepared with a full knowledge of all other nutrition literature being used by other agencies in order that duplication and conflicting viewpoints may be avoided.

4. Cooperate actively with other agencies dealing with different aspects of the nutrition problem. Offer the specialized services of the health department to other agencies to help them in dealing with their particular phases of nutrition.

5. Take an active part in the work of the state nutrition committee.

6. Offer information, consultation, guidance and encouragement to local health departments in developing local nutrition programs and in cooperating with the local nutrition committees.

7. Promote staff education in nutrition, including facilities for professional education in public health nutrition, and education of county and city health department personnel in nutrition activities.

8. Assist in sponsoring conferences and refresher courses in nutrition and related fields for public health and school personnel. During the past three summers nine such cooperatively sponsored six week conferences have been held in one state. Similar projects have been successfully carried out in several other states.

9. Active participation of nutritionists in the public health nursing and dental hygiene program, in well child clinics, in school health programs and in other activities of the maternal and child health division.

10. Include nutrition in the industrial hygiene program not only by nutrition education in the plant, but also by improving plant feeding facilities and the nutritional quality of the meals served.

11. Cooperate with and assist the state food distribution administrator in locating and meeting local food problems.

12. Take an interest in school lunch programs. The United States Public Health Service can consider requests for nutritionists for these programs under title VI funds if recommended

169. Sebrell, W. H., and Wilkins, Walter: The Role of the Health Department in the National Nutrition Program, Pub. Health Rep. **58**: 803 (May 21) 1943.

and requested through local and state health departments. Under rationing we should give more attention than ever to the adequacy of the meals our children get at school.

LOCAL HEALTH DEPARTMENT ACTIVITIES

1. Learn what other agencies have done and are doing within the area.
2. Affiliate with the local nutrition committee.
3. Study the nutritional status and needs of the area from medical and public health angles and help orient other agencies in this regard.
4. Distribute and interpret nutrition teaching material, especially material which deals primarily with local problems.
5. Have a planned program for staff education in nutrition within the department or in cooperation with other agencies.
6. Exert a stabilizing influence and interpret sound nutrition practices to the public, avoiding fads and extremes.
7. Interpret local nutritional conditions to the public through talks, newspaper articles, radio programs and so on.
8. Make an effort to increase the interest of local medical and dental professions in local nutrition problems and practical solutions.
9. Develop nutrition educational facilities for patients who attend public health clinics. In some places it may be advisable to establish clinics to deal primarily with nutrition problems.
10. Develop and maintain a movie, film strip, and slide library on nutrition and related subjects.
11. Encourage public eating places to serve food of good nutritional value and to prepare their foods in such a way as to conserve vitamins and minerals. This might be started as a consultation service.
12. Encourage civic clubs to sponsor programs which, either directly or indirectly, will improve the nutrition status of groups within the community.
13. Advise and sponsor feeding facilities in connection with child day care programs.
14. Stress nutrition in school health programs:

(*a*) Cooperate with teachers, parent-teachers associations and lunchroom managers in improving school lunches.
(*b*) Sponsor cooperative school lunch programs.
(*c*) Encourage the use of simple, wholesome, home prepared foods in lunchboxes rather than the use of "store bought" snacks.
(*d*) Watch for and stress nutritional deficiencies in physical examination of school and preschool children.
(*e*) When practical, conduct or sponsor demonstrations with school children showing results of improved nutrition (properly integrated with other health habits).
(*f*) Sponsor "sampling surveys" of school children for nutritional status. If possible, get local medical and dental societies to cooperate.

From a national point of view the state of nutrition of a considerable part of the population of this country is unsatisfactory and has been so for many years. Whether even this present state of nutrition can be maintained in the face of the present food situation depends on the efficiency with which we produce, distribute and utilize our food supplies. The signs and symptoms of malnutrition are often overlooked or attributed to other causes. Gross deficiency disease still exists, and the relationship of nutrition to other health problems is not common knowledge as it should be. Poor methods of using, preserving and preparing foods both in homes and in public eating places are responsible for tremendous losses in food values. Even in the face of food shortages there is as yet little tendency to conserve and use every bit of edible food. The uses of alternate foods when shortages exist is little appreciated. A shortage in beef results in a public clamor to satisfy the palate although physiologic needs can be met easily from other food sources without difficulty.

There is probably more public interest in nutrition and food today than ever before. Physicians and health officers can play an enormously important part in the national effort to improve nutrition by guiding this interest along sound lines. Too often the busy physician finds it easier to prescribe a vitamin pill than to investigate food habits and recommend dietary changes. Health officers need to become acquainted with the nutrition work being done by other agencies and have their staff members take their proper place in the nutrition program after they have obtained a background of knowledge of the work being done by other organizations.

We have an unparalleled opportunity in the field of preventive medicine. If agriculture is to be based on the nutritional needs of the population, health and medical authorities should determine what those needs are. Satisfactory nutrition depends on health and agricultural authorities working together. Agriculture up to now has had to assume the major portion of the burden of solving our nutritional problems. It is past time for medical and health authorities to assume their share of the responsibility.

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# *Council on Pharmacy and Chemistry*

## REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

AUSTIN E. SMITH, M.D., Secretary.

### NOMENCLATURE OF ENDOCRINE PREPARATIONS

Considerable progress has been made in the last few years on the development of potent endocrine preparations for clinical purposes. The standardization of these products has been significantly improved of late and promises to be established on a satisfactory basis. Nevertheless there is still confusion in the minds of physicians regarding the identity of many of these products, their sources and potencies. One of the factors most responsible for this unsettled state is the retention of proprietary terms for these products. The Council has made several appeals for a scientific nomenclature and has taken numerous steps in this direction so that therapy with endocrine preparations would not necessitate an intimate knowledge of the detailed lists of products. In the 1942 edition of Glandular Physiology and Therapy the chapter on "Present Status of Commercial Endocrine Preparations" discussed the therapeutic value of the various endocrine preparations together with a listing of the products accepted by the Council. No attempt was made, however, to note the proprietary names of other than products accepted by the Council except by their scientific terminology. The Council now considers it advisable to furnish physicians with the names and synonyms of these endocrine preparations which have been shown to have therapeutic effects. The present report was prepared, therefore, in order to enable physicians to clarify in their minds the nature of the various products, both proprietary and nonproprietary, together with the synonyms, basis of standardization and sources. The Council reserves the privilege of omitting from this list those preparations which are acknowledged by authorities to be of little value in endocrine therapy because of their unscientific nature, lack of sufficient potency or other evidence indicating little rationale for their use. The reader is referred to an article by W. A. Schonfeld (*New York State J. Med.* **42**:1538 [Aug. 15] 1942) who, in writing a somewhat similar article, has included preparations which the Council does not see fit to list for the reasons mentioned. In the present report the reader is advised that preparations are being omitted which are marketed by firms which have no products accepted by the Council in order to eliminate an excessive amount of effort and time in examining these multitudinous products. Such omissions do not necessarily imply a disapproval of certain of these products. The fact that

products are included in the appended list is, on the other hand, no indication that the Council approves of all of them. As a matter of fact, some of these products have been rejected by the Council. The reader is referred to chapter XXXI of Glandular Physiology and Therapy (THE JOURNAL, Oct. 4, 1941, p. 1175) for brief discussions on the actions and uses of some of the preparations described in the following list:

[NOTE.—Products marked with an asterisk have been accepted by the Council for inclusion in New and Nonofficial Remedies.]

## THYROID GLAND

### DESICCATED THYROID

Source: Obtained from domesticated animals that are used for food by man. Assay: Chemical—U. S. P. standard requires from 0.17% to 0.23% of iodine in thyroid combination.

PRODUCT AND FIRM

*Thyroid U. S. P. Marketed by eight or more firms.
Thyroid Emplets—iodine 0.3% assayed 50% above U. S. P. Parke, Davis.
Thyroid Tabloid—iodine 0.4% (net wt.) 5 grains equal 2 grains U. S. P. Burroughs-Wellcome.
Note: Avoid unstandardized products.

### THYROXIN (Natural)

Source: Active principle obtained from thyroid gland. Assay: Chemical—U. S. P. requires not less than 64% iodine in thyroxine molecule.

PRODUCT AND FIRM

*Thyroxin Crystals (intravenous). Squibb.

### THYROXIN (Synthetic)

PRODUCT AND FIRM

*Synthetic Thyroxin (intravenous and oral). Hoffmann-La Roche.

### THYROXIN FRACTION

Source: Disodium salt of thyroxin. Assay: Chemical—contains stated weight of thyroxin.

PRODUCT AND FIRM

*Tablets Thyroxin Fraction (oral). Squibb.

## PARATHYROID HORMONE[1]

### PARATHORMONE

Source: Animal parathyroid gland. Assay: U. S. P. units.

PRODUCT AND FIRM

*Parathyroid Extract. Lilly.
*Parathyroid Hormone. Squibb.
*Paroidin. Parke, Davis.

## ADRENAL CORTEX

### ADRENAL CORTEX EXTRACT

Source: Adrenal gland of animals. Assay: Biologic units (1 cc. of extract is derived from 40 Gm. of fresh gland).

PRODUCT AND FIRM

*Adrenal Cortex Extract. Upjohn.
Adrenal Cortex Extract. Wilson Laboratories.
Cortin. Roche-Organon.
Eschatin. Parke, Davis.

### DESOXYCORTICOSTERONE ACETATE

Source: Synthetic. Assay: Weight.

PRODUCT AND FIRM

Cortate. Schering.
Doca. Roche-Organon.
Percorten. Ciba.

## ADRENAL MEDULLA

### EPINEPHRINE

Source: Active principle of adrenal medulla; natural or synthetic (levorotatory). Assay: Chemical—U. S. P. standards.

PRODUCT AND FIRM

(Prepared for hypodermic, intravenous and oral medication).
*Suprarenalin. Armour.
*Adrenalin. Parke, Davis.
*Epinephrine. Upjohn; Wilson and other firms.
*Suprarenin. Winthrop.

### SOLUTION OF EPINEPHRINE HYDROCHLORIDE U. S. P. 1:1,000

Composition: Epinephrine in distilled $H_2O$ and hydrochloric acid—1:1,000.
*Products: Marketed by nine or more firms.

### SOLUTION OF EPINEPHRINE HYDROCHLORIDE U. S. P. 1:100

Composition: 1 part of epinephrine hydrochloride U. S. P. in 100 parts of isotonic solution of sodium chloride.

PRODUCT AND FIRM

*Suprarenin Solution 1:100. Armour.
*Solution of Adrenalin Chloride 1:100. Parke, Davis.

### SUSPENSION OF EPINEPHRINE IN OIL 1:500

Composition: A 0.2% suspension, containing 1 part epinephrine U. S. P. to 500 parts vegetable oil.

PRODUCT AND FIRM

*Epinephrine in Oil 1:500. Endo Products; Lakeside; Smith-Dorsey; Squibb.
*Adrenalin in Oil 1:500. Parke, Davis.

## PANCREAS

### INSULIN (Crystalline)

Source: Beef and pork pancreas. Assay: Biologic—solution of zinc insulin crystals standardized as follows: 1 mg. contains 22 insulin units as defined by Insulin Committee of University of Toronto.

PRODUCT AND FIRM

*Insulin; U 20, U 40, U 100. Sharp & Dohme.
*Insulin; U 20, U 40, U 80, U 100. Squibb.
*Iletin; U 20, U 40, U 80, U 100. Lilly.

### PROTAMINE ZINC INSULIN

Composition: A suspension of the precipitate of insulin, protamine and zinc in buffered solution. Assay: As above, with additional chemical assay.

PRODUCT AND FIRM

*Protamine Zinc Insulin; U 40, U 80. Sharp & Dohme; Squibb.
*Protamine Zinc and Iletin; U 40, U 80. Lilly.
NOTE.—Standard label colors: U 20, yellow; U 40, red; U 80, green; U 100, orange.

## ESTROGENS (CRYSTALLINE)

### ESTRONE—Theelin—Ketohydroxyestrin

Source: Urine of stallions and pregnant mares. Assay: International standard (0.0001 mg. equals 1 international unit).

PRODUCT AND FIRM

*Estrone in Oil. Abbott; Lilly.
*Estrone Suppositories. Abbott; Lilly.
Estrone Aqueous Suspension. Abbott.
*Theelin in Oil. Parke, Davis.
*Theelin Suppositories. Parke, Davis.
Theelin Aqueous Suspension. Parke, Davis.

### ESTRIOL—Theelol—Trihydroxyestrin

Source: Urine of pregnant women. Assay: Weight.

PRODUCT AND FIRM

*Estriol Capsules. Abbott; Lilly.
*Theelol Capsules. Parke, Davis.

### ESTRADIOL—Dihydroxyestrin

Source: Chemical modification of estrone from the urine of stallions and pregnant mares. Assay: Weight or biologic units.

PRODUCT AND FIRM

Dimenformon Ointment. Roche-Organon.
Dimenformon Tablets. Roche-Organon.
Ovocylin Ointment. Ciba.
Ovocylin Suppositories. Ciba.
Ovocylin Tablets. Ciba.
Progynon DH Ointment. Schering.
Progynon DH Suppositories. Schering.
Progynon DH Tablets. Schering.

### ESTRADIOL BENZOATE

Source: Esterification of estradiol. Assay: Weight or biologic units.

PRODUCT AND FIRM

Ben-Ovocylin in Oil. Ciba.
Dimenformon Benzoate in Oil. Roche-Organon.
Progynon B in Oil. Schering.

### ESTRADIOL DIPROPIONATE

Assay: Weight.

PRODUCT AND FIRM

Di-Ovocylin in Oil. Ciba.
Progynon DP in Oil. Schering.

## ESTROGENS (NONCRYSTALLINE)

### ESTROGENS—Estrogenic Substances—Essentially Estrone

Source: Urine of stallions or pregnant mares. Assay: In equivalents of international units.

PRODUCT AND FIRM

*Amniotin. Squibb.
*Amniotin Capsules. Squibb.
*Amniotin Suppositories. Squibb.
Estrogenic Hormone in Oil (from human placenta). National Drug.
Estrogenic Hormone in Oil. U. S. Standard Products Co.
*Estrogenic Substance. Sharp & Dohme.
Estrogenic Substance Solution. Breon.
*Solution of Estrogens. Lakeside Laboratories.
*Tablets of Estrogens. Lakeside Laboratories.
Estromone in Oil. Endo Products.
Estromone Ointment. Endo Products.
Estromone Tablets. Endo Products.

1. See also Activated Sterols. Source: Ergosterol, irradiated product. Viosterol in Oil: See list in N. N. R. Hytakerol (dihydrotachysterol, formerly known as A. T. 10), Winthrop.

Folestrin in Oil. Armour.
Menformon in Oil. Roche-Organon.
Menformon Ointment. Roche-Organon.
Menformon Tablets. Roche-Organon.
Ova-Estrin in Oil. Hospital Liquids.
*Solution of Estrogenic Substances. Smith-Dorsey.

ESTRONE SULFATE (Essentially)
Source: Urine of pregnant mares. Assay: Weight.

PRODUCT AND FIRM

Premarin Tablets. Ayerst, McKenna & Harrison.

ESTRONE AND ESTRIOL GLUCURONIDE (Essentially)
Source: Urine of pregnant women. Assay: Biologic units.

PRODUCT AND FIRM

Emmenin Liquid. Ayerst, McKenna & Harrison.
Emmenin Tablets. Ayerst, McKenna & Harrison.

## ESTROGENS (SYNTHETIC)

DIETHYLSTILBESTROL (Stilbestrol)—4'4' hydroxy-diethyl stilbene
Assay: Weight.
Marketed by numerous firms—a number are Council accepted.

DIETHYLSTILBESTROL DIPROPIONATE
Assay: Weight.

PRODUCT AND FIRM

Estrobene Dipropionate. Ayerst, McKenna & Harrison.
Diethylstilbestrol Dipropionate. Winthrop.

HEXESTROL—Dihydro-diethylstilbestrol
Source: Synthetic. Assay: Weight.
Marketed by The Wm. S. Merrell Co.

OCTOFOLLIN—2,4-di(p-hydroxyphenyl)-3-ethyl hexane
Assay: Weight.

PRODUCT AND FIRM

Octofollin. Schieffelin.

## PROGESTINS

SYNTHETIC PROGESTERONE (CRYSTALLINE)
Source: Synthesized from stigmasterol. Assay: Weight or international standard (1 mg. equals 1 international unit).

PRODUCT AND FIRM

Lutocylin in Oil. Ciba.
Progesterone in Oil. Armour.
Progestin in Oil. Roche-Organon.
Prolutin in Oil. Schering.
Nalutron. Winthrop.

SYNTHETIC PROGESTERONE (NONCRYSTALLINE)
Source: Synthetic. Assay: Biologic units converted into international units.

PRODUCT AND FIRM

Progestin in Oil. Abbott.
Lutromone in Oil. Endo Products.

NATURAL PROGESTERONE (NONCRYSTALLINE)—Progestin
Source: Animal ovaries. Assay: Biologic units converted in some instances to international units (1 Corner-Allen rabbit unit equals approximately 1 international unit).

PRODUCT AND FIRM

Lipo-Lutin in Oil. Parke, Davis.
Progesterone in Oil. Breon.
Progestin in Oil. Lilly; Upjohn.

PREGNENINOLONE (Anhydro-Hydroxy-Progesterone) (Oral)
Source: Synthetic. Assay: Weight.

PRODUCT AND FIRM

Luto-Cylol Tablets. Ciba.
Pranone Tablets. Schering.
Progesterol Tablets. Roche-Organon.

## ANDROGENS

TESTOSTERONE PROPIONATE
Source: Synthetic. Assay: Weight.

PRODUCT AND FIRM

Neo-Hombreol in Oil. Roche-Organon.
Neo-Hombreol Ointment. Roche-Organon.
Oreton F Ointment, Toplicators (testosterone). Schering.
Oreton in Oil. Schering.
Perandren in Oil. Ciba.
Perandren Ointment. Ciba.

METHYL TESTOSTERONE (Oral)
Source: Synthesized from testosterone. Assay: Weight.

PRODUCT AND FIRM

Metandren Tablets. Ciba.
Neo-Hombreol (M) Ointment. Roche-Organon.
Neo-Hombreol (M) Tablets. Roche-Organon.
Oreton M Tablets. Schering.
Oreton M Ointment. Schering.

## PITUITARY GLAND PRODUCTS

NOTE.—All of the following products are derived from extracts of the anterior pituitary glands of domesticated animals which are used for food by man.

ANTERIOR LOBE FACTORS
Adrenotropic, Lactogenic, Thyrotropic: Further clinical investigation is necessary before these products can be marketed with assurance of effective potency.

GROWTH PROMOTING FACTOR
Assay: Biologic—in terms of rat growth units which as yet have not been made uniform.

PRODUCT AND FIRM

Polyansin (contains growth, gonadotropic and thyrotropic principle). Armour; Ayerst, McKenna & Harrison.
Phykentrone (P). Squibb.
Antuitrin-growth. Parke, Davis.
Phyone. Wilson.
Growth-Complex. Armour; Ayerst, McKenna & Harrison.

GONADOTROPIC FACTOR
Assay: Biologic—rat units which are not yet uniform.

PRODUCT AND FIRM

Maturity Extract (Gonadotropic). Armour.
Gonadotropic Factor. Ayerst, McKenna & Harrison.
Gonadophysin (P). Searle.
Prephysin (P). Chappel.
(These products contain follicle stimulating and luteinizing hormones.)

POSTERIOR LOBE (WHOLE)
Solution of Posterior Pituitary. Assay: Biologic—U. S. P. standardization. 0.1 cc.—1 U. S. P. posterior pituitary unit.

PRODUCT AND FIRM

*Ampoules Post. Pit. Sol. Abbott.
*Pituitary Liquid. Armour.
*Pituitary Extract. Lilly; Endo; Lakeside; Merrell; Squibb; Upjohn; U. S. Standard; Wilson.
Infundin. Burroughs-Wellcome.

POSTERIOR PITUITARY POWDER
Assay: U. S. P.—1 mg. equals 1 U. S. P. posterior pituitary unit.

PRODUCT AND FIRM

*Desiccated Post. Pit. Powder U. S. P. (used as snuff). Armour; Lilly; Parke, Davis.

POSTERIOR PITUITARY FRACTION
Vasopressor and antidiuretic. Assay: Biologic—pressor units.

PRODUCT AND FIRM

*Pitressin. Parke, Davis.
*Oxytocic. Assay: Biologic—oxytocic units.

PRODUCT AND FIRM

*Pitocin. Parke, Davis.

EQUINE GONADOTROPIN
Source: Serum of pregnant mares. Assay: International units (0.1 mg. of international standards equals 1 international unit).

PRODUCT AND FIRM

Anteron (P). Schering.
Gonadin. Cutter.
Gonadogen (P) in powder form—dissolved for injection. Upjohn.

CHORIONIC GONADOTROPIN
Source: Urine or placenta of pregnant women. Assay: International or biologic units (0.1 mg. of the international standard equals 1 international unit).

PRODUCT AND FIRM

Anterior Pituitary-Like Gonadotropic Hormone. Lakeside Laboratories.
Anterior Pituitary-Like Sex Hormone. Hospital Liquids; U. S. Standard Products.
Antuitrin-S. Parke, Davis.
A. P. L. Ayerst, McKenna & Harrison.
Chorionic Gonadotropin. Breon.
Entomone. Endo Products.
*Follutein (P). Squibb.
Gestasel. National Drug.
Korotrin (P). Winthrop.
Pranturon (P). Schering.
Pregnyl (P). Roche-Organon.
NOTE.—(P) In powder form—dissolved for injection.

In preparing these lists of products an extended attempt was made to keep abreast of the changes constantly being made in the marketing of these preparations. However, errors may be found because of changes in products which have escaped the notice of the Council's office or because of the introduction of new agents since the preparation of this report.

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SATURDAY, OCTOBER 9, 1943

## COUNCIL STANDARDS AND MEDICAL ADVERTISING

Among the most important steps for the advancement in the United States of the practice of scientific therapy was the establishment of the Council on Pharmacy and Chemistry by the American Medical Association. The Council on Pharmacy and Chemistry was organized to protect the medical profession and the public against fraud, undesirable secrecy and objectionable advertising in connection with proprietary medicinal articles. A proprietary article means any chemical, drug or similar preparation used in the treatment of disease and protected against free competition as to name, product, composition or process of manufacture by secrecy, patent, copyright or other means. Notwithstanding the wholly laudable character of these functions, the creation of the Council was met by a furor of opposition from manufacturers, salesmen and the venal medical press which derived from this unsavory business profits tainted by their origin from the helpless sick and the dying. Patients must depend on their doctors for the choice of remedies. Doctors depended then on the information that came to them in the pages of medical publications and on information derived from detail men. Only too often even those pages of periodicals devoted to allegedly scientific contributions could be influenced if not purchased by the advertising that appeared in the same issue. No wonder that the establishment of a council of physicians, pharmacologists, chemists, physiologists and other qualified scientists to sift truth from falsehood and to give physicians a dependable source of information on new and nonofficial remedies should have elicited a shrieking and a moaning and a groaning from those who saw in its functioning their impending dissolution.

In almost thirty-five years that have passed since the Council came upon the scene, its results have justified the far sighted efforts of Philip Mills Jones, Frank Billings, George H. Simmons, Reid Hunt, Lafayette Mendel, Torald Sollmann and other medical and basic science leaders who gave so freely of their time and their wisdom to its work. Again and again the medical leaders of foreign nations have written in envy of the ability of the Council to achieve the results it seeks. The subsequent creation of Councils on Foods and Nutrition and on Physical Therapy has been an indication of the approval of the House of Delegates.

In the years that have passed, more and more manufacturers of pharmaceutical preparations have given their collaboration and support to the work of the Council on Pharmacy and Chemistry. Many medical schools in their teaching of therapeutics limit themselves to the products listed in Useful Drugs. The book New and Nonofficial Remedies, a list of the preparations investigated and accepted by the Council, is increasingly used as a reference in medical schools and hospitals. The new legislation which controls foods and drugs developed from national acceptance of the principles so long maintained by the Council; no longer is it possible to launch a new remedy on the American public without previous controlled clinical testing. Such governmental control is, however, concerned only with harmlessness, and not with efficacy or advertising of the product. All the more need, therefore, for the work of the Council.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, under the direction of the Board of Trustees, limits its acceptance of advertising to products that have been accepted by the Council. All advertising for Council-accepted products is submitted to the Council on Pharmacy and Chemistry for consideration prior to publication. Most of the state medical journals and several independent medical journals also restrict their acceptances of advertising similarly. Such support is necessary to maintain the strength of the Council. Formerly some of the state medical journals were the private property of physicians, publishers or corporations that had founded them. They were conducted largely for financial gain or personal prestige. Gradually ownership changed; today in most instances these publications are the property of the state medical associations which publish them.

Outside the periodicals published by medical organizations are some which do not limit their acceptance of advertising in any easily apparent way. Their pages are replete with the announcements of remedies that have not met the criteria of scientific evaluation. Conspicuous examples of this type are the throw-away publications, such as *Medical Economics* and *Modern Medicine,* sent free to physicians because their support comes from the publication of advertising which could not gain entrance into periodicals of recognized scientific origin and merit.

The journals of two state medical societies—Illinois and New York—have been conspicuous almost from the first in their insistence on the profits to be derived from the publication of advertisements of unaccepted products. For a brief period the *New York State Journal of Medicine* agreed to abide by scientific therapy; apparently

the insistence of the business office ultimately prevailed; that periodical is today among those counted as lost before the altar of those who give their faith to scientific therapy.

In 1913 the Board of Trustees of the American Medical Association, in its desire to aid and support the work of the Council on Pharmacy and Chemistry and to aid those medical periodicals which wished to enlist themselves in this righteous cause, created the Cooperative Medical Advertising Bureau. Year by year the reports of the Bureau have appeared and have indicated the extent to which the Bureau has been helpful in securing advertising for the state medical journals and increasing their income. Recently there seems to have been a lessening of the careful scrutiny of advertising copy that is necessary in limiting advertising strictly to Council-accepted products. In the past month, for instance, the *Pennsylvania Medical Journal* has carried announcements of perandren and metandren, male sex hormones which have not been accepted, and of privine, a vasoconstrictor used for nasal inhalation; the *New England Journal of Medicine* carried one for ferrosate, which is a mixture used against anemia. *California and Western Medicine* in the July issue alone published advertisements for six nonaccepted products. Indeed, almost any issue of any journal may have one or more advertisements that do not meet Council Standards. The September issue of the *Southern Medical Journal* carries advertisements for more than twenty unaccepted preparations, and the Illinois and New York journals continue to be veritable directories of unestablished and unscientific therapy.

As long as any considerable part of the medical profession contributes to extending the blight of the falsely exploited proprietary medicine, the battle for scientific therapy remains difficult. In any war the most dangerous attack is the attack from the rear. The threat most difficult to meet is that from those who should be presumed to be friends. The time should long since have passed when leaders of medical organizations consent to permit the exploiters of unestablished proprietary remedies to pay the bulk of printing and publishing bills of the medical journals that are supposed to represent scientific medicine. Can the physicians of Illinois and New York and the representatives of a few states who are urging a breakdown of the Council standards believe that the business managers of their periodicals are better equipped to judge what is good in materia medica and therapeutics than is the Council on Pharmacy and Chemistry? Fortunately for American medicine, the vast majority of the profession has not accepted that point of view. The governing bodies of the medical societies of Illinois and New York and the Councils and boards of trustees of the other medical societies which are being urged by business managers to depart from the standards of the Council might well give more consideration to their responsibility to scientific medicine. The good name and prestige of American medicine have come from its support of scientific remedies and ethical practice, from its condemnation of fraudulent and unscientific nostrums and of commercialized medicine. That good name gives us strength before the bar of public opinion where the point of view of scientific medicine needs to prevail. Let us keep the good name unsullied; its value is far above that of jewels or gold.

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## REACTIONS FOLLOWING SPINAL PUNCTURE

Reactions have been variously reported as occurring in 17 to 40 per cent of patients after lumbar puncture. The syndrome includes headache accompanied in severe cases by vertigo, nausea and vomiting. The most characteristic feature of this headache is the prompt relief that ensues when the patient lies down, and return of the headache when he sits up. The headache may be transitory, lasting one or two hours; moderate, terminating in one or two days; or severe, lasting six or more days. Sicard and others suggested that the headache was due to leakage of the cerebrospinal fluid into the epidural space through the defect in the dura left by the puncturing needle. The cerebrospinal fluid in a closed sac forms a pad for the brain and the spinal cord. At the base of the brain this pad acts as a cushion or water bed. MacRobert [1] argued that the cushion is absent when the patient sits up and the weight of a good part of the brain is suddenly imparted through the pons to the communicating plexus of veins. The blood about to leave the skull is impeded and is forced to turn back and travel by other crowded pathways. The resulting congestion causes a sudden rise of venous pressure. The relief of headache when the patient lies down is due to the fall of pressure when the weight is removed from the plexus of veins resting on the clivus of the occipital bone. The proponents of the leakage theory urged that the patient be confined to bed with the head lowered for twenty-four to forty-eight hours. Of the 30 patients thus treated, MacRobert records the occurrence of severe headache in 12 (40 per cent). Jacobaeus and Frumerie [2] and later Nelson [3] found that there was a significant fall in the spinal fluid pressure between the time of the spinal puncture and the onset of the headache, suggesting reduction in the volume of the blood, probably through leakage. Nelson developed an ingenious method of plugging the puncture hole in the meninges with a strand of catgut. Of 102 cases in which this was practiced, typical postpuncture reaction developed in only 5 (4.9 per cent). Of 92 cases in which spinal

1. MacRobert, R. G.: The Cause of Lumbar Puncture Headache, J. A. M. A. **70**: 1350 (May 11) 1918.
2. Jacobaeus, H. C., and Frumerie, K.: About the Leakage of the Spinal Fluid After Lumbar Puncture and Its Treatment, Acta med. Scandinav. **58**: 102, 1923.
3. Nelson, M. O.: Postpuncture Headaches: A Clinical and Experimental Study of the Cause and Prevention, Arch. Dermat. & Syph. **21**: 615 (April) 1930.

puncture was concurrently made in the usual manner, typical postpuncture reaction developed in 16 (17.4 per cent).

The leakage theory and the theory of meningeal irritation have been questioned recently by observers who have found that patients who were not put to bed after the puncture had less reaction than those who were treated by bed rest. Adler [4] argued that a patient in the upright position should have greater leakage and therefore more severe headache. Blau [5] reported that 21.2 per cent of patients who rested in the clinic and at home had reactions of a severe nature. Of those who left the clinic immediately but rested all day at home 21.7 per cent had severe reactions, but of those who did not rest at all only 6.4 per cent reacted severely. He concludes that the best method of preventing postpuncture reactions is the use of a fine needle and keeping the patient active for a considerable time after the puncture. Adler encouraged his patients to stay erect as long as possible after the puncture. Out of a group of 108 patients 14 (13 per cent) had a moderate or severe reaction. Of 10 men who went to bed immediately after the puncture, 7 (70 per cent) had moderate to severe reaction. Of 20 men who went to bed eight hours after the puncture, 2 (10 per cent) had slight and 2 (10 per cent) mild reactions; none had either moderate or severe reactions. Of 38 men who went to bed six hours after the puncture, only 2 (5 per cent) had severe or moderate headache. Adler therefore believes that the leakage and the meningeal irritation theories do not explain the reaction. He concludes that the cause of the headache is increased intracranial hypertension due to reaction of the choroid plexus caused by emotion. He points to the fact that Kulchar and King [6] were able to reduce the incidence of typical postpuncture headache from 25.5 per cent to 13.5 per cent in 105 patients by the administration of 3 grains of sodium amytal by mouth before puncture. Schube and Le Drew [7] reported a diminution in the incidence of reactions following lumbar puncture by administration of 3 grains of sodium amytal. Adler found a definite relationship between constitutional inadequacy and headache. Davenport [8] likewise suggests that lack of physical stamina and increased suggestibility, as evidenced in the higher incidence of reactions among females and Puerto Ricans in his large series, are factors. Adler believes that the predominant factors in the causation of postpuncture headache are the constitutional make-up of the patient and psychogenic influences.

Consideration of the several theories advanced and of the contradictory facts presented suggests that further studies will be required to elucidate the mechanism of the postpuncture headache and its successful prevention.

4. Adler, Harry: A Study of the Headaches Following Diagnostic Spinal Taps, New York State J. Med. **43**: 1328 (July 15) 1943.

5. Blau, Albert: Reactions Following Spinal Puncture, Urol. & Cutan. Rev. **45**: 239 (April) 1941.

6. Kulchar, G. V., and King, A. D.: Use of Sodium Amytal in Prevention of Reactions Associated with Lumbar Puncture, Arch. Neurol. & Psychiat. **30**: 170 (July) 1933.

7. Schube, P. G., and Le Drew, Frederick: The Prevention of Reactions Due to Lumbar Spinal Puncture, New England J. Med. **211**: 537 (Sept. 20) 1934.

8. Davenport, K. M.: Postpuncture Reactions: A Clinical Study, New York State J. Med. **39**: 1185 (June 15) 1939.

## *Current Comment*

### THE EPIDEMIOLOGY OF SCARLET FEVER

An epidemic disease can be most satisfactorily investigated by studying the community in which the outbreak occurs throughout the preepidemic, epidemic and postepidemic periods. Such an investigation was carried out near Iasi (or Jassy) in Rumania in 1936 under the auspices of the International Health Division of the Rockefeller Foundation and the Iasi Institute of Hygiene.[1] The city in the province of Oltanea had a population of about 100,000. The field work was done in the villages surrounding the city. The area was primarily agricultural, the inhabitants living for the most part in small villages and proceeding to their farm work each day in the surrounding countryside. The studies demonstrated a rough semilogarithmic relationship between the degree of latitude and the incidence of scarlet fever in that latitude. It has been suggested that this relationship may be due both to climatic conditions and to a lower susceptibility of those races which populate the tropical regions. The studies showed that the streptococcus flora of a community during nonepidemic periods includes many different strains, almost constantly changing their relative proportions. Persons up to 20 years of age are more frequently carriers than are adults. The types of streptococci which are prominent in causing scarlet fever one year may gradually assume an insignificant role and be replaced by other types. During epidemics a single type is generally responsible but this may vary, depending on whether an outbreak occurs in a community free from scarlet fever or is superimposed on previously existent endemic disease. A type of streptococcus which causes scarlet fever may also cause other forms of streptococcic illness. The types of streptococci most frequently recovered from persons with scarlet fever and other streptococcic diseases are those most commonly found in normal carriers in the same community. This suggests that the pathogenesis may be related to the degree of distribution of the organisms throughout the community. The number of cases of scarlet fever which occur is related to the carrier rate for the epidemic type. The distribution of cases of scarlet fever by age coincides with the age distribution of positive Dick tests, except that the peak for the former is with children from 5 to 9 years old and for the latter from 1 to 4 years old. Antitoxic immunity is accepted, and, with few exceptions, Dick negative persons are immune to the clinical syndrome of scarlet fever. Antibacterial immunity may also be a factor. The principal conclusion from this study is that the amount of illness caused at any one time by a given strain of streptococcus

1. Schwentker, F. F.; Janney, J. H., and Gordon, J. E.: The Epidemiology of Scarlet Fever, Am. J. Hyg. **38**: 27 (July) 1943.

is determined by three factors: the current pathogenic ability of the strain, the degree of dispersal throughout the community and the specific immune status of the population. These factors are all labile and their constant change accounts for the variations with time in the amount of streptococcic disease. Following the outbreak of war in Europe it was necessary to remove the collected material to New York and to complete the studies in the laboratories of the International Health Division there. This is, of course, only one example of the tremendously disruptive force of war on medical research.

## HAIR LACQUER PADS—A WARNING

Information has come to the office of THE JOURNAL to the effect that certain hair lacquer pads, widely used by women throughout the United States to make the hair conform to recent styling or "up-do," have been causing dermatitis or severe inflammations of the skin around the back of the neck and ears. Cases have come to the attention of physicians in many cities. The Food and Drug Administration, immediately on notification, made a preliminary investigation which, according to reports reaching THE JOURNAL, indicates that the irritative action results from a change in the formula of manufacture of the products under investigation by the inclusion of a new gum. It may take some time to identify this ingredient accurately. With the usual alertness and efficiency that have characterized its activties the Food and Drug Administration has issued a request for the recalling of hair lacquer pads manufactured by Hubère Cosmetics of Chicago and of the Parfait Powder Puff Company, an Illinois corporation. Under the circumstances, women will do well to discontinue the use of these hair lacquer pads until their harmlessness has been established.

## ANTHIOMALINE IN CLINICAL MEDICINE

Anthiomaline is lithium antimony (trivalent) thiomalate prepared as a 6 per cent solution, 1 cc. of which contains about 0.01 Gm. of antimony. An analysis of the extensive pharmacologic and experimental studies has just become available.[1] The drug has been employed therapeutically in venereal lymphogranuloma, granuloma inguinale, schistosomiasis, leishmaniasis, filariasis, trypanosomiasis, febrile jaundice, multiple sclerosis and trachoma. Therapeutic dosage depends on the disease to be treated, as do some of the toxic reactions to the drug. Its approximate range of therapeutic effectiveness was indicated by early experiences with venereal lymphogranuloma. It has been proposed to begin with 60 mg. injected intramuscularly and to increase the dose of the single injections to a possible maximum of 300 mg. until a total dose of between 2 and 4 Gm. has been reached. Injections ordinarily are given three times a week, and repetition is advisable after an interval of several weeks. The maximum dose for a single injection may be determined by the appearance of rheumatoid pains, which constitute the most widely observed toxic reaction. The pains may be localized or general; they appear several hours after injection and they usually last twenty-four hours and occasionally longer. Painful swellings at the site of the injection sometimes occur. Salivation, retching, vomiting and abdominal pains have been observed. Slight fever, headache, thirst and fatigue may also appear in the course of treatment. Venereal lymphogranuloma is the condition in which anthiomaline has been used most extensively, some 250 cases having been recorded in the literature. Excellent results were obtained in 35 to 75 per cent, and failures have been encountered in from 10 to 25 per cent of the patients treated. Experience with granuloma inguinale has been too scanty to warrant conclusions, although the results appear promising. Anthiomaline treatment of filariasis on a small number of patients has on the whole been disappointing. Good results have been uniformly reported with the use of this drug in more than 130 cases of genitourinary schistosomiasis. The efficacy of anthiomaline in cases of leishmaniasis is extremely doubtful. Thirty-three cases of trypanosomiasis have been treated with a combination of moranyl and anthiomaline with consequent sterilization of lymph and blood and reports of cure of fifteen months' duration in 17 cases. From the information available it may be concluded that anthiomaline has a considerable variety of therapeutic usefulness and a sufficiently low toxicity to warrant its further clinical trial.

1. A Summary of Current Literature on Anthiomaline, National Research Council, Division of Medical Sciences, Prepared by the Office of Medical Information, Aug. 18, 1943.

## HEALTH AND THE "VICTORY CORPS"

The United States Office of Education, sponsoring the Victory Corps in high schools, has published the proceedings of a committee of physicians and educators convened by the Office of Education to outline preparation of teachers for the program of physical fitness through health education.[1] The shortage of school personnel for health education led the United States Commissioner of Education to consider the possibility of giving supplementary training to science teachers and to teachers of home economics and physical education. The committee [2] met in May and formulated standards which teachers should meet if they are to be expected to function in the health education program. These standards, in general, indicate that persons having medical knowledge, such as doctors, are not usually equipped pedagogically, and vice versa. The findings and recommendations of the committee, which should be of interest to physicians and educators, and especially to physicians serving as public health officials in school health programs or as members of boards of education, are available in a reprint [1] from the official biweekly publication of the United States Office of Education, "Education for Victory." Inquiry should be addressed to the United States Office of Education, Federal Security Agency, Washington, D. C.

1. Reprint Education for Victory, Official Biweekly of the United States Office of Education, Federal Security Agency, Washington, D. C. 1, June 15, 1943.

2. W. W. Bauer, M.D., William H. Bristow, Lillian Davis, Bess Exton, Edna Gerken, Ruth E. Grout, Philip G. Johnson, Ray Kauffer, Dorothy La Salle, Margaret Leonard, Leon R. Meadows, Florence O'Neil, Jackson R. Sharman, Sherwood D. Shankland, Frank Stafford, Clair E. Turner, Jennie Wahlert, R. W. Webster and Charles C. Wilson, M.D., chairman.

# MEDICINE AND THE WAR

*In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.*

## ARMY

### AVIATION MEDICAL EXAMINERS

Graduation exercises were held at the School of Aviation Medicine, Randolph Field, Texas, on August 26 following completion of the course for aviation medical examiners. The didactic portion of the course was conducted at the School of Aviation Medicine, Randolph Field, Texas, and the practical portion of the course at the three army air forces classification centers. The list of students graduating follows:

ALABAMA

James P. Collier, Major, Tuscaloosa.
Albert H. Green, Major, Birmingham.
Elias N. Kaiser, Major, Montgomery.
James H. Meigs, Captain, Anniston.
Dayrel D. Smith, Captain, Birmingham.

ARIZONA

John S. Mikell, Major, Tucson.
William G. Shultz, Major, Tucson.

ARKANSAS

Barnett P. Briggs, Captain, Little Rock.

CALIFORNIA

Charles Benninger Jr., Captain, Oroville.
Henry C. Bernstein, Captain, San Francisco.
Norman C. Fox, 1st Lieut., San Bruno.
William A. Gannon, 1st Lieut., Pasadena.
Herbert Greenhood, Major, Oakland.
Millard E. Gump, Major, Oakland.
Gordon C. Hall, 1st Lieut., Soledad.
Ronald L. Hughes, 1st Lieut., Los Angeles.
Jesse J. Iverson, 1st Lieut., San Francisco.
Maxwell S. Kassel, 1st Lieut., Hondo.
Frederick G. Kirby, 1st Lieut., Los Angeles.
Edward A. Kirz, 1st Lieut., Butte Meadows
Arthur L. Kobal, 1st Lieut., Los Angeles.
Donald O. McGowan, Major, Los Angeles.
Newell L. Moore, Major, Santa Ana.
Ralph E. Netzley, Captain, Pasadena.
Maurice J. Regan, 1st Lieut., Los Angeles.
Frederick G. Reynolds, Captain, Los Angeles.
George H. Rue, 1st Lieut., Riverside.
Lawrence A. Solberg, 1st Lieut., Kerman.
Milo K. Tedstrom, Major, Santa Ana.
George E. Webster, 1st Lieut., Inglewood.
Harris R. Wilson, Captain, Modesto

COLORADO

Robert K. Dixon, Major, Denver.
Bryce D. Smith, 1st Lieut., Denver.

CONNECTICUT

George A. Burnie, 1st Lieut., Danbury.
George R. Eckert, 1st Lieut., Danbury.
Ronald H. Kettle, Major, Norwich.
Royal A. Meyers, Major, Watertown.
Victor G. H. Wallace, Major, Darien.

DELAWARE

Constance A. D'Alonzo, 1st Lieut., Wilmington.

DISTRICT OF COLUMBIA

George F. Baier III., Lieut. Col., Washington.
John Louzan, Captain, Washington.
Leo H. Mugmon, 1st Lieut., Washington.

FLORIDA

Anthony J. Barranco, 1st Lieut., Lake Wales.
Albert D. Kistin, 1st Lieut., Bay Pines.
Carl C. Mendoza, 1st Lieut., Jacksonville.
Robert J. Needles, Major, St. Petersburg.
Murray M. Reckson, 1st Lieut., Miami.
Francis C. Skilling, Major, Miami
Frank L. Snyder, Captain, Hollywood.
Cyrus H. Stoner, Major, Fort Pierce.

GEORGIA

Braswell E. Collins, Captain, Waycross.
Gordon L. Green, Major, Mount Berry.
Oscar H. Lott, Captain, Savannah.
William B. Turk, Captain, Nelson.

IDAHO

John H. Culley, 1st Lieut., Idaho Falls.
Frederick H. Haigler Jr., Major, Boise.

ILLINOIS

Raymond H. Abrams, 1st Lieut., Chicago.
Marvin F. Austin, Major, Chicago.
Ben H. Barbour Jr., 1st Lieut., Centralia.
George W. I. Bard, 1st Lieut., Sheldon.
Merrill C. Beecher, 1st Lieut., Knoxville.
Carl A. Gebuhr, 1st Lieut., Evanston.
John W. Gray, Captain, Geneva.
Anton P. Huml, 1st Lieut., Peoria.
Roland F. K. Jordan, Captain, Pekin.
Herbert Kahan, Captain, Chicago.
Emerson C. Kunde, Captain, Woodstock.
Robert C. Long, 1st Lieut., Chicago.
Cornelius E. Murphy, Captain, Chicago.
Oliver Rian, Captain, East Peoria.
Frederick J. Ricketts, Captain, Sadorus.
Percy J. Ross, Major, Chicago.
Lee H. Schlesinger, Major, Hines.
Edward J. Schmehil, 1st Lieut., Chicago.
Albert Sheade, 1st Lieut., Chicago.
Everett L. Strohl, Major, Chicago.
Charles R. Sugden, Captain, Deerfield.
Sydney W. Tauber, 1st Lieut., Chicago.
Scottie J. Wilson, 1st Lieut., Urbana.

INDIANA

Victor F. Albright, 1st Lieut., Indianapolis.
Clarence E. Bunge, Captain, Logansport.
Robert M. Dearmin, Major, Indianapolis.
Floyd L. Grandstaff, Captain, Decatur.
Howard E. Hill, Major, Muncie.
Howard H. Marks, Captain, Evansville.
Raymond J. Modjeski, Captain, Hammond.
Frederick H. Simmons, Captain, Goshen.
Robert A. Staff, Captain, Rockville.
Charles O. Weddle, 1st Lieut., Lebanon.

IOWA

Harold C. Bastron, Major, Red Oak.
Daniel F. Crowley, Captain, Des Moines.
Frank D. Edington, Colonel, Spencer.
Robert H. Foss, 1st Lieut., Remsen.
Edwin B. McConkie, Major, Cedar Rapids.
Kermit W. Myers, 1st Lieut., Sheldon.
Merlin R. Wyatt, Captain, Manning.

KANSAS

Charles H. Johnson, 1st Lieut., Kinsley.
Charles R. Magee, 1st Lieut., Wichita.

KENTUCKY

Harry S. Andrews, Major, Louisville.
Horace W. Carle Jr., 1st Lieut., Louisville.
Arthur C. McCarty, Major, Louisville.
John K. Mack, Captain, Louisville.
Lawrence T. Minish Jr., Major, Frankfort.
Edgar C. White, Captain, Louisville.
Earl P. Wright, Captain, Pikeville.

LOUISIANA

John J. Burdin, 1st Lieut., Lafayette.
John Corso, 1st Lieut., Independence.
Parker K. Hughes, Captain, New Orleans.
Julien C. Pate Jr., Captain, New Orleans.
Salvadore J. Russo, 1st Lieut., New Orleans.
Alvin Stander, Captain, Baton Rouge.

MAINE

Harry Butler, Major, Bangor.
Louis C. Lesieur, Captain, Biddeford.

MARYLAND

Walter E. Yingling, Major, Baltimore.

MASSACHUSETTS

Timothy E. Allen, Captain, Arlington.
Harwood W. Cummings, Captain, Greenfield.
Howard H. Englander, 1st Lieut., Boston.
John J. Kelleher Jr., 1st Lieut., Lawrence.
John E. Smith, 1st Lieut., East Weymouth.
Knowlton D. Stone, Captain, Greenfield.
Roland P. Wilder, 1st Lieut., Malden.

MICHIGAN

Herschel L. Browns, Captain, Ann Arbor.
Frederick W. DeYoung, Captain, Spring Lake.
Robert E. Fallis, Captain, Kalamazoo.
Willard E. Fischer, 1st Lieut., Wyandotte.
Neil A. Gates Jr., Captain, Ann Arbor.
Jason (NMI) Hodges, 1st Lieut., Detroit.
Arvid G. Holm, Captain, Three Rivers.
Clinton H. McKay Jr., 1st Lieut., Ann Arbor.
Philip T. Mulligan, Captain, Mount Clemens.
Jesse P. Muse, 1st Lieut., Detroit.
John E. Patrick, 1st Lieut., Detroit.
Lelland J. Rather, 1st Lieut., Detroit.
Walter F. Sethney, Captain, Menominee.
Everette M. Steffes, 1st Lieut., Detroit.
Kenneth N. Wells, 1st Lieut., Spring Lake.
Stewart C. Wheeler, 1st Lieut., Detroit.

MINNESOTA

Harold J. Frank, Captain, New Prague.
Richard B. Graves, 1st Lieut., Red Wing.
Bernard N. Karleen, 1st Lieut., Balaton.
Paul C. Leck, Captain, Austin.
Joseph J. Mack, Lieut. Col., St. Paul.
Robert E. Mattison, 1st Lieut., Minneapolis.
Jan H. Tillisch, Captain, Rochester.

MISSISSIPPI

Randolph L. Clark Jr., Captain, Jackson.

MISSOURI

Charles H. Barnett Jr., 1st Lieut., Kansas City.
Victor K. Hager, 1st Lieut., St. Louis.
Aretus D. Martin, 1st Lieut., Sikeston.
John B. Ryan, 1st Lieut., Kansas City.
Hugh R. Smith, 1st Lieut., St. Louis.
William D. Susanka, 1st Lieut., St. Louis.

MONTANA

Robert G. Lemon, Captain, Glendive.
Leland G. Russell, Captain, Billings.

NEBRASKA

William R. Malony, Captain, Omaha.
Edwin J. Shaughnessy, 1st Lieut., North Platte.

NEW JERSEY

Jules E. Baime, 1st Lieut., Newark.
Joseph F. Corless, Major, West New York.
Allan B. Crunden Jr., Captain, Jersey City.
Gerald B. Demarest, 1st Lieut., Westfield.
Philip D. Gilbert, Captain, Camden.
Joseph J. Kohn, 1st Lieut., Trenton.
Thomas A. Masciocchi, Captain, Orange.
Meyer Notkin, Captain, Paterson.
Salvatore S. Piacente, Captain, Jersey City.
Charles G. Prather, Captain, Westwood.
Richard Wagner, 1st Lieut., South Orange.

NEW YORK

Jules B. Aaron, Captain, Brooklyn.
Adrian R. Avitabile, Captain, Brooklyn.
Raymond K. Bush, Major, Mount Vernon.

Joseph M. Covelli, Captain, Flushing.
Martin J. Coyne, 1st Lieut., Geneva.
Maurice M. Croll, 1st Lieut., Brooklyn.
Martin Cutler, Captain, Brooklyn.
Salvatore A. Dispenza, 1st Lieut., Lackawanna.
John A. Failla, 1st Lieut., New York.
Max M. Goldenkranz, Captain, Brooklyn.
Eugene L. Griffin, Captain, New York.
Wilfred Guerra, 1st Lieut., Brooklyn.
John A. Hamilton Jr., 1st Lieut., Brooklyn.
Archie M. Harris, Captain, Rockville Centre.
Myron L. Kenler, 1st Lieut., Maspeth.
John C. Kilroe, Major, New York.
George G. Knight, 1st Lieut., Piermont.
Edgar A. Lawrence, Captain, New York.
Lewis B. London, Captain, New York.
William G. MacDonald, 1st Lieut., New York.
Habeeb Z. Maroon, 1st Lieut., New York.
Joseph H. Merin, Captain, Botton Landing.
Saul Michalover, Major, Brooklyn.
Myron J. Miller, Captain, New York.
Walter W. Miner Jr., Major, Baldwin.
Holger C. Nelson, Captain, Watertown.
Alfred H. Rifkin, 1st Lieut., New York.
Carl C. Rosenberg, 1st Lieut., Brooklyn.
Emanuel V. Rumore, Captain, Brooklyn.
Julius J. Sachs, 1st Lieut., New York.
Jacob Schneider, Captain, Brooklyn.
John E. Sullivan, Major, New York.
Estel G. Surber, Captain, Brooklyn.
John H. Wadsworth, Captain, Cobleskill.
Milton A. Wald, 1st Lieut., Brooklyn.

NORTH CAROLINA

Roderic O. Jones, 1st Lieut., Burnsville.
Robert E. Stone, Captain, Chapel Hill.

OHIO

Nicholas G. Amato, 1st Lieut., Cincinnati.
Jack J. Berry, 1st Lieut., Cleveland.
Robert F. Corwin, Major, Dayton.
Arthur F. Dorner, Major, Akron.
James A. Ellery, 1st Lieut., Shelby.
Glen K. Folger, Major, Cleveland.
Reuben H. Hamman, 1st Lieut., Waterville.
John R. Harding, Major, Cincinnati.
Francis J. Heringhaus, Major, Mansfield
Charles S. Higley, Major, Cleveland.
George F. Hilles, Captain, Cleveland Heights.
Harold L. Keiser, 1st Lieut., Fremont.
Howard Lauer, 1st Lieut., Dayton.
William R. Liebschner, 1st Lieut., Deshler.
Earl D. McCallister, Captain, Chillicothe.
John Miglionico, 1st Lieut., Cleveland.
Morris S. Osherwitz, Captain, Cincinnati.
Adolph B. Schneider Jr., Captain, Cleveland.
John R. Schroder, 1st Lieut., Cincinnati.
Malcolm E. Switzer, 1st Lieut., Galion.
Harold O. Tagett, Captain, Rock Creek.
Stanley W. Whitehouse, 1st Lieut., Cincinnati.

OKLAHOMA

George E. Dodson, Captain, Muskogee.
Willard D. Holt, 1st Lieut., Altus.
Roy L. Neel, Captain, Oklahoma City.
Charles R. Rayburn, Lieut. Col., Norman.
John R. Smith, Captain, Oklahoma City.

OREGON

Richard I. Rich, 1st Lieut., Woodburn.
Robert P. Schefter, 1st Lieut., Portland.

PENNSYLVANIA

Harold S. Agnew, 1st Lieut., Ben Avon.
Daniel A. Atkinson Jr., 1st Lieut., West View.
Harold P. Belknap, Captain, York.
Maurice L. Brown, 1st Lieut., Philadelphia.
Nicholas L. Ciaccia, Captain, Pittsburgh.
Anthony N. Domonkos, 1st Lieut., Huntingdon.
Walter C. Ferer, Captain, Conneaut Lake.
George E. Fissel, Captain, Philadelphia.
Robert T. Gillis, Captain, Tarentum.
George L. Greaser, Major, Altoona.
Duncan S. Hatton, Captain, Chester.
Willard W. Hayne, Captain, Paullina.
Hubert B. Haywood Jr., 1st Lieut., Abington.
Samuel S. Huntzberger, 1st Lieut., Sinking Springs.
Nathan Katsiff, 1st Lieut., Philadelphia.
Luther A. Lenker, 1st Lieut., Harrisburg.
James F. MacDonald, 1st Lieut., Pittsburgh.
Joseph L. Magrath, Major, Upper Darby.
John L. Meyers, 1st Lieut., Shillington.
Jack M. Orman, 1st Lieut., Philadelphia.
William D. Prescott, 1st Lieut., Pine Grove.
Charles L. Sacks, 1st Lieut., Philadelphia.
Charles Schnall, Captain, Philadelphia.
Roman V. Ulane, 1st Lieut., McAdoo.
Jay E. Weidenhamer, 1st Lieut., Punxsutawney.

RHODE ISLAND

Richard Rice, Captain, Providence.

SOUTH CAROLINA

Abram E. Adams, Captain, Greenwood.

SOUTH DAKOTA

George R. Dornberger, Major, Miller.

TENNESSEE

Robert M. Conger, 1st Lieut., Lexington.
Marshall B. Lynch, 1st Lieut., Memphis.
John C. Turley, 1st Lieut., Memphis.

TEXAS

Arthur B. Alexander, Captain, Spur.
Alfred C. Bennett, Captain, Marlin.
Herman R. Buzbee, 1st Lieut., Dallas.
Hamilton F. Ford, Captain, Galveston.
William C. Ghormley, 1st Lieut., Corpus Christi.
Frederick J. Koberg, 1st Lieut., Big Spring.
John W. Lanius, 1st Lieut., Dallas.
Gordon Phillips, 1st Lieut., Haskell.
Marcus A. Pierson, Captain, Galveston.
Nellins C. Smith, Captain, Hillsboro.
D. D. Wall, Captain, San Angelo.
Stephen W. Wilson, 1st Lieut., Linden.

UTAH

Kurt E. Rose, 1st Lieut., Salt Lake City.

VERMONT

Joseph B. Crowley, 1st Lieut., Brattleboro.
Paul C. Willard, 1st Lieut., Montpelier.

VIRGINIA

James L. Davis, Captain, Raccoon Ford.
Edward M. Holmes Jr., Major, Richmond.
Hulburt C. McCoy, 1st Lieut., Gordonsville.
Charles D. Schilling, Captain, Charlottesville.
Frank A. Zack, 1st Lieut., Newport News.

WASHINGTON

Donald D. Corlett, Major, Seattle.
Frank J. Cornelius, Captain, Olympia.
Harry A. Gilbert, Captain, Mount Vernon.
Russell B. Hanford, Captain, Spokane.
Albert D. Haug, Captain, Wenatchee.
Charles W. Hoffman, 1st Lieut., Wauwatosa.
William C. Kintner Jr., Captain, Seattle.
Lumir M. Mares, Captain, Wenatchee.
Lloyd H. Smith, 1st Lieut., Wenatchee.
Rudolph E. Stuart, 1st Lieut., Spokane.

WEST VIRGINIA

James E. McClung, 1st Lieut., Richwood.
Robert A. McLane Jr., 1st Lieut., Arthurdale.
Richard N. O'Dell, 1st Lieut., Belle.

WISCONSIN

William F. Cormack, 1st Lieut., Wausau.
Max F. Drozewski, 1st Lieut., Milwaukee.
Rollie M. Harrison, Captain, Boscobel.
Erwin J. Jelenchick, 1st Lieut., Milwaukee.
Robert G. Kvarnes, 1st Lieut., Superior.
Robert C. Love, Captain, Glenwood City.

HOME ADDRESS UNKNOWN

Juan Benavides, Lieut. Comdr., Peruvian Army.

## DOCTORS OPERATE UNDER SHELLFIRE

Following is a dispatch as printed in the Chicago *Sun*, September 24, from the United Nations Headquarters in North Africa:

Three delicate operations of brain surgery were performed successfully in a tent among the sand dunes of Salerno during the critical days when the Germans had the entire Fifth Army bridgehead under artillery fire, it was revealed today.

Lieut. Col. Paul K. Sauer of New York Hospital took his contingent ashore amid a rain of German lead.

Exhausted by two days and nights of bombing, strafing and mortar fire, the men of the evacuation hospital finally organized their scattered equipment and spent all night setting up portable operating rooms and tent walled wards on a field not far inland. Then the tired staff began a twenty-four hour schedule of operations and treatment.

Major Howard A. Patterson of New York, former surgeon at Roosevelt Hospital and a veteran of the Tunisian campaign, led his surgical staff in a round the clock schedule, with three teams working in succession on never empty operating tables.

Nurses were not due to be landed for several days, so the hospital's enlisted men donned operating gowns and sterilized masks and worked long hot hours in operating tents. Many had no more than two hours' sleep in the first three days.

Casualties that piled up during the first week of the campaign made expansion necessary, so a surgeon was added and then tents from a medical battalion. Abdominal punctures, head wounds, fractures and burns formed the bulk of the hospital cases.

## COLONEL DABNEY AWARDED LEGION OF MERIT

Col. Albert S. Dabney, M. C., U. S. Army, who recently relinquished his duties as assistant commandant of the Medical Field Service School, Carlisle Barracks, Pennsylvania, was awarded on September 15 the Legion of Merit for meritorious conduct and outstanding service. The presentation was made by Brig. Gen. Addison D. Davis, commandant of the school. It read in part as follows:

"Col. Albert S. Dabney, M. C., U. S. Army. For exceptionally meritorious conduct in the performance of outstanding service. From the beginning of the emergency until the end of 1941 he has been director of the Medical Department Equipment Laboratory, where by his conspicuous energy and ability he developed many new major articles of equipment needed by the Medical Department for war. Since Jan. 1, 1942, as assistant commandant of the Medical Field Service School, he has had immediate charge of training approximately 14,000 Medical Department officers and officer candidates. His careful supervision of their instruction, his unremitting devotion to duty and his knowledge have resulted in giving these officers the essentials of their duties for the field, thus contributing to the success of the United States in the present war."

With twenty-seven years of service to his credit, Colonel Dabney already holds decorations from the American, British, French and Haitian governments, as well as numerous other military ribbons. He was recently appointed assistant dean of the University of Pittsburgh School of Medicine, where he took up his duties on October 1.

### SOLDIER'S MEDAL AWARDED TO ARMY NURSE

The War Department announced on September 1 the award of the Soldier's Medal to 2d Lieut. Margaret M. Decker, Army Nurse Corps, the second woman ever to receive this award, for heroism at Topaz, Calif., on June 19, 1943, when, according to the citation accompanying the award, while swimming in the Colorado River, without regard for her safety she went to the rescue of a soldier and saved him from drowning. Though physically exhausted, Lieutenant Decker administered first aid to the soldier and accompanied him to a station hospital, where he was given medical attention. Lieutenant Decker entered the army on Nov. 19, 1942. She is a graduate of the St. Barnabas Hospital School of Nursing, Newark, N. J., 1938, and is assigned to the 127th Station Hospital, Desert Training Center, California.

### PRISONERS OF THE JAPANESE

According to the Chicago *Tribune* of August 12, Lieut. Amiel L. Palermo, formerly of Chicago, is a prisoner of the Japanese. A card received recently by his mother indicated that he is being held a prisoner in the Philippines in prison No. 1. Lieutenant Palermo graduated from the University of Illinois College of Medicine, Chicago, in 1940 and entered the service on July 5, 1941.

According to the New Albany (Indiana) *Ledger* of September 3, word has been received from Capt. Thomas H. Hewlett, formerly of Washington, D. C., that he is safe and well. Captain Hewlett has been held a prisoner of the Japanese since the fall of Corregidor. He graduated from the University of Louisville School of Medicine in 1938 and entered the service in April 1941.

According to the Stanton (Mich.) *Clipper Herald*, word has been received from 1st Lieut. Arthur L. Benison, former physician in the Edmore Hospital, Edmore, Mich., who is being held a prisoner of the Japanese. Lieutenant Benison, who graduated from the University of Michigan Medical School, Ann Arbor, in 1937, was a member of a medical unit stationed in the Bataan Peninsula.

## PROCUREMENT AND ASSIGNMENT SERVICE FOR PHYSICIANS, DENTISTS AND VETERINARIANS

### QUOTAS OF INTERNS AND RESIDENTS

Since many hospitals have not returned their questionnaires, it is impossible at this time to give every hospital its quota of interns and residents. It was therefore felt advisable to release this memorandum through THE JOURNAL so that the state chairmen for the Procurement and Assignment Service and the hospital superintendents would have this additional information concerning the nine-nine-nine program. As soon as the hospitals in each state have been appraised, the state chairmen and the hospital superintendents will be notified of the definite quota which appears as a blank in paragraph two of the following release from the Directing Board:

1. The new intern-resident program based on reduction in the length of internships to nine months and deferment by the Army and Navy of commissioned interns to serve as residents begins Jan. 1, 1944, for nine month periods. This program consists of:

Nine months internship.
Nine months junior residency.
Nine months senior residency.

This program applies to all interns and residents who will have completed nine months of hospital service on or after Jan. 1, 1944. Deferments from active duty which have already been approved by the Army or Navy for residents will be continued to the date authorized.

2. Quota for ——— hospital:

——— internships for nine months period.

——— combined number junior and/or senior residencies for nine months (major portion should be junior residents so that some of them can be retained in senior residencies for nine months period).

Adjustments of this quota may be authorized by the directing board of the Procurement and Assignment Service but will be made only under exceptional circumstances and on the recommendation of the state chairman of the Procurement and Assignment Service.

3. These quotas include all interns and all residents who will serve the institution, including those physically disqualified or otherwise ineligible for military service and those interns who are commissioned officers but who automatically are deferred by the military services for their nine month internships and those residents who are deferred for nine months for either a junior or a senior residency.

4. Failure to limit staffs to these allocated numbers will result in preventing the Procurement and Assignment Service from requesting the Surgeon General to defer commissioned officers to fill essential residencies in the institution.

5. The greater the number of vacancies filled with applicants who are physically disqualified or otherwise ineligible for military service, the more certain is the maintenance of the house staff; therefore no requests for deferment of commissioned officers should be considered until every effort has been exhausted to fill the vacancies with individuals ineligible for military service.

6. For the deferment of a commissioned officer to fill an essential residency, form number 218 should be completed in triplicate and forwarded to the state chairman of the Procurement and Assignment Service for his approval and submission through the central office to the surgeon general of the service in which the applicant holds a commission. Attention is called to the necessity of the individual recommended for deferment to indicate his desire to accept this appointment by personal signature in the space provided.

7. Hospitals should make contacts and appointments of prospective interns and residents in the usual manner. The Procurement and Assignment Service has no authority to assign interns and residents to hospitals; hence this assignment of an allowable quota is no guaranty that a hospital will be able to procure that number of interns or residents. Hospitals may notify the central office of the Procurement and Assignment Service of vacancies in authorized internships and residencies. This office will arrange for the publication of this information so that individuals who are available and interested may apply for such positions.

8. Certain junior residents who are commissioned officers may be deferred for a third nine months to serve as senior residents within the limitation of authorized quotas. Selection of junior residents and of senior residents may be made from interns and junior residents respectively serving in the same hospital or in other hospitals.

9. Commissioned officers who are to serve as junior or senior residents for nine month periods should be selected at least four months before the termination of their current deferments. Form No. 218 must be submitted promptly for all such individuals in order that deferments may be authorized for the issuance of orders to active duty. Requests for deferment received after orders have been issued cannot be approved.

10. Any questions concerning this announcement or the nine-nine-nine program should be addressed to the state chairman of the Procurement and Assignment Service and not, under any circumstances, to the Office of the Surgeon General.

# CIVILIAN DEFENSE

## NEED FOR PROTECTIVE SERVICES IN TIME OF WAR

A memorandum recently issued by the Office of Civilian Defense, Washington, D. C., to regional medical, nursing, engineer, gas and rescue officers states that rumors that civilian defense is no longer necessary have recently been spread by irresponsible persons. These rumors are thoughtless or calculatingly subversive, for they are not supported by Army authorities responsible for our coastal defenses or by the present military situation. Fortunately the success of our armed forces overseas has saved us thus far from experiencing the horrors of enemy bombing to which the cities of our allies are being subjected. In the opinion of the best military authorities our coastal areas and industrial centers will not be free of the danger of enemy attack from the air or of widespread sabotage until the last day of the war.

Civilian defense is also needed as one of the essential measures for safeguarding internal security. This is especially true of the Emergency Medical Service. If we had not created a nationwide organization for civilian defense two years ago, we would be obliged to organize one today for home security. Disasters of all kinds have increased as the result of the tremendous speeding up of our great industries, the overburdening of our railroads and the inexperience of hundreds of thousands of new war workers. Our police, fire departments, public works and utility services and our hospitals, on which we depend for protection, are being increasingly depleted of trained personnel. We must therefore strengthen our voluntary protective services throughout the land. Along the Pacific and the Atlantic coasts these services must be especially strong in volunteer personnel and equipment to guard us against the hazards of enemy attack and sabotage until that day when the Army itself advises us that the danger is ended.

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## MOBILIZATION OF EMERGENCY MEDICAL SERVICE ON AIR RAID ALERTS

The Office of Civilian Defense, Washington, D. C., issued on September 13 Circular Medical Series No. 33 on the "Mobilization of the Emergency Medical Service on Air Raid Alerts," in which the different colored warning signals are explained as follows:

*Yellow Warning Signal.*—The chief of Emergency Medical Service and his deputies assigned to duty at control centers should receive the yellow warning and proceed immediately to their designated posts. All casualty receiving hospitals should receive the yellow warning, which should be relayed immediately to the administrator, the superintendent of nurses and the chief engineer.

*Blue Warning Signal.*—1. Mobile medical teams: (*a*) Teams composed of resident personnel of hospitals prepare for action by assembling, with equipment, at a designated point in the hospital and stand ready for orders from the control center. (*b*) Teams composed of persons from the neighborhood of a hospital assemble at the hospital. (*c*) Teams designated to assemble at casualty stations remote from a hospital report to the casualty station. 2. Stretcher teams: Stretcher teams on call assemble at their posts of duty at hospitals or casualty stations. 3. Ambulance teams (driver and attendant): (*a*) Teams composed of persons on duty at a hospital or depot at which the ambulance is parked prepare their vehicles and equipment for action. (*b*) Teams composed of persons residing in the neighborhood of hospitals or ambulance depots assemble at the hospital or depot at which they are on call. 4. Hospital personnel: The following will report to the hospitals to which assigned: physicians on shock, surgical triage, fracture or other emergency teams; anesthetists; nurses and volunteer nurse's aides on call at the time for emergency duty; hospital protection personnel such as wardens, fire guards, messengers and essential maintenance personnel. In preparing hospitals for action, every effort should be made to reduce to a minimum the movement through streets. Hospital administrators and chiefs of staff should therefore determine their minimal requirements and recommend emergency personnel for membership in the U. S. Citizens Defense Corps or the Civilian Defense Auxiliary Group. The chief of Emergency Medical Service should arrange for the appointment, training and proper identification of such emergency personnel.

*Red Warning Signal.*—Members of the Emergency Medical Service stand by at their posts throughout the red warning period until dispatched to incidents or casualty stations on orders from the control center. The physician in charge of a mobile medical team at a hospital or casualty station may send forward a stretcher team or other personnel to nearby incidents on his own initiative.

*Omission of Yellow or First Blue Warning.*—The sudden or rapid approach of enemy planes may prevent the giving of either the yellow or blue warning, or both. In the event that a red warning is given without preliminary warnings, Emergency Medical Service personnel will immediately take the action normally taken on the yellow and blue warnings.

*Blue Warning Signal Following Red.*—Emergency Medical Service personnel remain at assigned posts or at posts to which they have been dispatched until relieved by the chief of Emergency Medical Service.

*All Clear.*—Emergency Medical Service personnel remain at their posts of duty until relieved by the chief of Emergency Medical Service.

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## HOSPITAL MEN VOLUNTEERS

The Office of Civilian Defense, Washington, D. C., issued on September 13 Operations Letter 140 to state and local defense councils for the attention of war services boards and volunteer offices, pointing out the acute shortage of manpower in hospitals throughout the country. The Office of Civilian Defense, in cooperation with the American Hospital Association, is working on a plan to promote the use of men volunteers in hospitals where they are needed. At a meeting of the American Hospital Association in Buffalo, September 13-17, the plan as outlined here was presented in order that hospital administrators might be able to hear from their own group what has already been done in some hospitals and how through their local defense councils they can secure help in recruiting men volunteers.

The Health Committee should be asked by the War Services Board to ascertain from hospital administrators the extent of their manpower problem. The Health Committee should appoint a special committee to do this job, and on this committee should be represented the principal hospitals, the Volunteer Office and the Publicity Committee of the Defense Council. If a serious shortage is found the committee should assist the hospitals to determine what assistance hospital men volunteers can give. The committee should then take the following steps:

1. Request the Volunteer Office to obtain men volunteers to work in hospitals.

2. Plan to publicize local needs for men volunteers through the publicity director of the local Defense Council and the Volunteer Office, using all appropriate mediums such as newspapers, the radio and speakers.

3. Plan with hospital administrators, the Volunteer Office and the Training Committee of the Defense Council for organizing hospital staffs for the proper use of volunteers, including provision for their training and supervision.

4. Arrange with the executive of the Citizens Service Corps for special induction ceremonies and awarding of insignia to the men hospital volunteers.

The Volunteer Office should be responsible for securing the hospital men volunteers. The following points will guide the Volunteer Office in fulfilling this responsibility:

1. The files should furnish the first source of volunteers. If there is not a sufficient number of suitable men registered, recruiting should be undertaken at once.

2. The general public can be reached most effectively through the press and the radio. Stories should indicate clearly what kinds of men volunteers are wanted, how many are needed, where they will work, and when and where interested men can be interviewed.

3. Medical schools and colleges provide another resource. Speakers should be sent to explain the need to such students,

and convenient arrangements should be made for interviewing interested men.

4. Organized men's groups, such as labor organizations, church groups, ministers' organizations, fraternal organizations and men's civic groups, are a potential source. Organizations of the clergy are an especially good source. Speakers should be made available to these men's organizations, and convenient arrangements should be made for interviews with interested applicants.

5. Selection from among men volunteers either enrolled or especially recruited should be carefully made on the basis of specifications of the various hospitals.

6. Referrals should be made directly to the hospitals as long as the hospitals' need for men volunteers continues to be unfilled.

7. Follow-up on referrals should be made to determine whether the hospitals are satisfied, and replacements should be made whenever necessary.

# MISCELLANEOUS

## U. S. CADET NURSE CORPS PROGRAM

According to the Division of Nurse Education, U. S. Public Health Service, Washington, D. C., expansion of housing and educational facilities will be necessary to many nursing schools if the required number of student nurses are to be enrolled in the U. S. Cadet Nurse Corps. Institutions which cannot finance the entire cost of such additions are eligible to apply for assistance under the Lanham act if they are participating in the Cadet Nurse Corps program. New construction must be avoided wherever possible by leasing or purchasing an existing building which can be suitably altered. Institutions applying for financial aid under the Lanham act should make a preliminary request to the regional office of the Federal Works Agency having jurisdiction in the state. Institutions which do not require financial assistance should make application for priorities assistance directly to the War Production Board, Washington, D. C., on form WPB 617. WPB 2814.1 will accompany WPB 617. In the "hospital section" of WPB 2814.1 only questions pertinent to the applicant hospital need be answered. In the "nurses' home" section, all questions must be answered.

## WARTIME GRADUATE MEDICAL MEETINGS

On October 14 a conference under the auspices of the Wartime Graduate Medical Meetings will be held at the Army and Navy General Hospital at Hot Springs, Ark., with Lieut. Col. Irving S. Wright, M. C., as chairman. The schedule will include papers entitled "Studies on the Mechanism of Recovery from Pneumococcic Pneumonia" by Dr. Barry Wood and "Allergy as It Is Related to Bronchial Asthma," with case presentations by Dr. Harry Alexander, and a round table in which Lieutenant Colonel Wright, Dr. Wood, Dr. Alexander and Major Dudley C. Ashton, M. C., will take part.

On October 7 a conference was held at the same hospital on "Malignant Diseases in Military Age."

Other recent programs under the auspices of the Wartime Graduate Medical Meetings have been held at the Station Hospital, Fort Sill, Oklahoma, and Will Rogers Field, Oklahoma City.

## RELIEF WINGS INCORPORATED

Relief Wings, Inc., with headquarters at 80 East 42d Street, New York City, is a nonprofit organization for aerial mercy aids to civilians. The air ambulance service which this institution conducts is offered to charity patients at a cost of 5 cents per mile. For those patients who are able to pay the full operating cost of the airplane a charge of 14 cents per mile is made to cover all necessary costs. Flight surgeons and flight nurses on registers throughout the United States who have been receiving aeromedical training on the care of the airborne patient are available.

Dr. Harry V. Spalding is chairman of the organization's Aero Medical Research Committee. Miss Ruth Nichols, well known aviatrix, is the executive secretary. Among the sponsors, officers, sectional leaders and advisory committees of Relief Wings, Inc., are nationally known citizens, aviators and scientists.

This organization is largely maintained by the donations which it receives, and contributions may be sent to Relief Wings, Inc., at 342 Madison Avenue, New York City.

## PUBLIC HEALTH UNDER HITLER

According to NDZ of July 12 the increased employment of women and the burdens thus placed on large families have made it necessary to extend the day nursery scheme and give more help to mothers of large families. The NSV needs assistance for these tasks. As far as it is not possible to meet this demand through normal channels, young girls will be called up for this purpose. This kind of war work is specially suited to the natural inclinations and interests of girls, as it consists exclusively of feminine tasks. It will not only enrich the knowledge and increase the ability of the girls but also in many cases inspire them in their choice of a vocation.

The reich youth leader, the general trustee for the direction of labor and the minister of education have issued the directives for this work in a joint decree. They say that, where in special cases the requirements cannot otherwise be met by the labor offices, girls of the seventh form of oberschulen can be made available. The present seventh form will be employed on this work until August 31. They will take their holidays from September 1 to 20 and will enter the eighth form on September 21. They will be relieved by the girls of the new seventh form. These girls will be employed from Sept. 1, 1943 until Feb. 26, 1944, at the latest.

The Social Welfare Office of the Reich Youth Directorate has been entrusted with the organization of this scheme. The girls may work, first, as assistants in day nurseries, in small harvest, agricultural and auxiliary kindergartens, and, secondly, in NSV recuperation institutions for juveniles and in connection with the Extended Child Evacuation Scheme. Where the need for assistants is fully covered, the girls may be employed to reinforce the NSV domestic help scheme locally or within the kreis. They must, however, be able to sleep at home. Before work of this kind is started there will always be parents' meetings at the schools, at which further details of the work will be announced. The cost of accommodation, food, insurance, fares and pocket money of 15 reichsmarks per month will be borne by the NSV.

*Nachrichten für den Aussenhandel* of May 17 states that, owing to shortage of fish in Bulgaria, food preserving factories have been temporarily prohibited to preserve fish. This measure was deemed necessary in order to provide the population with as much fresh fish as possible. Despite the efforts of the authorities, insufficient fish has been landed lately, especially on the Black Sea coast, where the industry has been greatly handicapped by war conditions. Fishing tackle has become scarce and is difficult to replace in wartime. In the opinion of the fishermen the relatively low prices are also partly responsible for the present shortage. An appeal for higher prices was refused by the authorities.

*L'Action française* of July 24 complains that children under 3 are not entitled to certain rationed food such as calf brain, liver, eggs and ham, which they need more than certain other categories. The birth rate is higher than five years ago, but too many infants die as a result of malnutrition. Since mothers have been encouraged to have more children, it is essential to feed the children properly.

The *Deutsche Zeitung in den Niederlanden* of July 14 states that 99 per cent of the doctors who wrote the second letter to Seyss-Inquart have apologized to him. They are said to have declared that many of the signatures were forged.

# ORGANIZATION SECTION

## MEDICAL ECONOMIC ABSTRACTS

### HOW MANY PHYSICIANS ARE NEEDED

The United States Public Health Service has made a questionnaire study on medical conditions in the District of Columbia, Baltimore City, certain Maryland counties and Georgia.[1] The average weekly patient load is shown in the following table:

| | Averages | | | |
|---|---|---|---|---|
| Place of Practice | Office | Hospital | Home Patient | Total |
| District of Columbia..... | 86 | 8 | 21 | 115 |
| Maryland: | | | | |
| Baltimore..... | 82 | 6 | 31 | 119 |
| Exclusive of Baltimore... | 96 | 7 | 29 | 132 |
| Total..... | 89 | 7 | 30 | 126 |
| Georgia: | | | | |
| Urban..... | 78 | 11 | 23 | 112 |
| Rural..... | 79 | 6 | 26 | 111 |
| Total..... | 79 | 7 | 25 | 111 |

The averages, however, are somewhat deceptive, as they vary greatly according to age. Physicians under 45, especially those from 35 to 44 inclusive, care for two to three times as many as those above 64 years of age. The number of patients that can be seen naturally varies with the proportion of office and home visits. With considerable variation the average office hours in Baltimore for physicians are between four and five, while in the counties outside they are about an hour longer. The same difference exists between urban and rural counties in Georgia.

An effort was made to determine the possible optimum patient load. Sixty per cent of urban general practitioners declared that they could increase the present load. The remainder declared that they are caring for as many patients at present as they could manage. Only forty-nine per cent of rural physicians thought that they could care for more patients. This would mean an increase from 112 and 111 patients for urban and rural general practitioners respectively to 135 and 128 patients. From these facts some general conclusions are drawn. It is calculated that the number of persons per physician cannot be increased beyond 1,200 to 1,500 in Maryland and 2,000 to 2,400 in Georgia. This conclusion, however, is affected by the fact that it is measured in both "need" for medical services and by the economic "demand," and it is not certain that this would not be changed if economic conditions improve, in Georgia, for example. "The ratio of physicians to population constitutes nothing more than index of the maximum amount of services that can be provided, but whether or not the physicians' potential services are fully utilized will depend not on their number but on the effective demand for services."

1. Ciocco, Antonio, and Altman, Isidore: The Patient Load of Physicians in Private Practice, Pub. Health Rep. **58:** 1329 (Sept. 3) 1943.

### AN OPTIMISTIC OUTLOOK

Recent bulletins of the Metropolitan Life Insurance Company bring a combined message of remarkable improvement in vital conditions in the United States. In the first place we learn that, "despite the hardships of war, American wage earners and their families are living on the average longer than ever before."

Not only are we living longer but there is a promise that there will be more of us since "a steady rise in the American birth rate since 1933 will have paid, by the end of this year, a dividend of 2,000,000 additional babies for the ten year period."

The added number of births is also accompanied by a striking decline in the maternal death rate, so that "childbearing in this country is now safer than ever before," since "only about one third as many American mothers currently lose their lives in childbirth as compared with ten years ago. About two maternal deaths per thousand live births now take place in the United States, while prior to 1934 the rate was between six and seven per thousand."

Meanwhile, although there has been a recent outbreak of cerebrospinal meningitis which was the most extensive in the country's history, "fortunately in 1943 we have a powerful weapon against this disease. The great majority of cases are now cured by the sulfa drugs, which have revolutionized the treatment of the disease. In the general population, prior to 1939, the proportion of deaths to cases was more than 40 per cent. . . . Preliminary data for 1942 for this country give a fatality rate only slightly more than 20 per cent. Where facilities for diagnosis and early treatment are better than average, fatality rates of 10 per cent or less are experienced. Indeed, in our army camps the rate has been only 3.5 per cent, as compared with 34 per cent in the first world war."

### NEW HAMPSHIRE PREPAYMENT PLAN

The house of delegates of the New Hampshire Medical Society, meeting at Concord, N. H., on September 12, accepted a report of a committee on medical economics giving a detailed outline of a prepayment nonprofit organization. This plan will include the rural areas and, according to a report in the *Union* (Manchester, N. H.), will provide for premiums that "will appeal to the lower and middle, as well as the higher income brackets." The organization will be known as the "Blue Shield" and will be administered through the New Hampshire Blue Cross Hospitalization Plan. The house of delegates authorized the medical economics committee to work out details for the establishment of a corporation.

The house of delegates also adopted a resolution condemning the Wagner-Murray-Dingell bill and stated that in its opinion the need for improvement in the distribution of medical care "can best be met by the extension of existing voluntary plans for medical and hospital care."

## MEDICAL LEGISLATION

### MEDICAL BILLS IN CONGRESS

*Change in Status.*—H. J. Res. 159 has passed the Senate, appropriating $18,600,000 for grants to states, including Alaska, Hawaii, Puerto Rico and the District of Columbia, to provide, in addition to similar services otherwise available, medical, nursing and hospital maternity and infant care for wives and infants of enlisted men of the fourth, fifth, sixth and seventh grades in the armed forces of the United States, under allotments by the Secretary of Labor and plans developed and administered by state health agencies and approved by the chief of the Children's Bureau. An additional appropriation of $20,000 was also made available for salaries and expenses of the Children's Bureau in carrying out the program.

The federal money that is made available for grants to states may be used for payments of commitments made prior to Oct. 1, 1943 for similar services to the wives and infants of enlisted men of the first, second and third grades of the armed forces.

# Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

## CALIFORNIA

**Alumni Research Foundation Created.** — The Alumni Research Foundation of the College of Medical Evangelists, Los Angeles, has been created by recent action of the board of directors of the Alumni Association and the board of trustees of the College of Medical Evangelists. The foundation is incorporated under the laws of California. While the primary purpose is to stimulate research, it may also accept gifts, grants, bequests and other forms of property to be used for charitable or educational purposes to aid the College of Medical Evangelists or advance medical science. At the first meeting of the board, August 8, the by-laws were ratified and Dr. Newton G. Evans, dean of the medical college, was elected president. The foundation consists of twelve to fifteen trustees.

## COLORADO

**Physician's Conviction Reversed by Supreme Court.**— Conviction of Dr. Philip L. Cobianchi, Denver, on the charge of performing an illegal operation, was reversed on August 3 by the Colorado Supreme Court, newspapers reported. It was stated that the evidence submitted "was insufficient to support the charge." Statements to the press indicated that the physician was convicted in 1942 on a charge of performing an illegal operation in 1941, the patient dying a few months later of peritonitis. The supreme court held that the pregnancy of the woman was not proved beyond doubt and testimony was that she had undergone an operation for appendicitis subsequent to the purported illegal operation. The newspaper reports stated that Dr. Cobianchi was sentenced to ten to twelve years for second degree murder. Newspaper accounts implied that the state will file a motion with the supreme court for a rehearing, the intimation being that the physician would be held on other charges still on file in the district court.

## FLORIDA

**Appointments in State Health Department.** — The appointment of Dr. Elmer J. Teagarden, Orlando, and Dr. Estella Lucille Johnson Marsh, Tallahassee, as directors of the state board of health's bureau of tuberculosis and bureau of maternal and child health, respectively, were reported on September 3. Dr. Teagarden has been serving as superintendent of the Morgan County Tuberculosis Sanatorium, Flint (Decatur P. O.), Ala., and succeeds Dr. Lynne E. Baker, Jacksonville, who resigned to enter private practice in Dayton, Ohio, last July. Dr. Marsh has been serving as chief physician at the Florida State College for Women, Tallahassee. Since the resignation of Dr. Robert C. Hood, Jacksonville, to enter private practice in Arlington, Va., the latter part of 1942, the bureau of maternal and child health has been in charge of Dr. Erwin F. Hoffman, director of the bureau of epidemiology.

## ILLINOIS

**Springfield Hospital Dedicated.**—The dedication of the new Memorial Hospital of Springfield took place September 26. The new building occupies a four block site and was erected at a cost of $1,800,000. It has 285 beds and 50 bassinets. Of brick construction with concrete trimming, the building is composed of a central tower ten stories high and three wings seven stories high. At the dedication exercises the speakers included Lieut. Col. Charles W. Mayo, M. C., A. U. S.; Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, on "What a Standardized Hospital Means to a Community"; Dr. Malcolm T. MacEachern, Chicago, associate director of the American College of Surgeons, and Dr. Warren P. Morrill representing George Bugbee, executive secretary, American Hospital Association, Chicago. The *Illinois State Journal and Register* devoted a special section, September 26, to a review of the hospital's development and to features emphasizing the modern installations and accommodations. The section also carried pages of congratulatory messages from local physicians and commercial and other firms.

### Chicago

**Dr. Wynekoop Refused Request for Freedom.** — Dr. Alice L. Wynekoop, who is serving the tenth year of her sentence for conviction in the murder of her daughter-ir-law, was denied a writ of habeas corpus by Federal Judge John P. Barnes, September 11, newspapers report. Dr. Wynekoop is serving a twenty-five year sentence in the women's prison at Dwight, Ill.

**Dr. Elvehjem Lectures on Vitamin B Complex.**—Conrad A. Elvehjem, Ph.D., professor of biochemistry, University of Wisconsin, Madison, will address the annual joint meeting of the Institute of Medicine of Chicago and the Chicago Society of Internal Medicine at the Palmer House on October 25. His subject will be "The Nutritional Significance of the Newer Members of the Vitamin B Complex."

**Dr. Bachmeyer Receives Hospital Award.**—Dr. Arthur C. Bachmeyer, director and associate dean of the biology division of the University of Chicago Clinics, was presented with the American Hospital Association's Award for meritorious service to the hospital field during a meeting of the association on September 13. According to the inscription on the medal constituting the award, Dr. Bachmeyer was recognized as a "distinguished administrator and educator whose achievements have greatly advanced standards of treatment for patients and educational opportunities of lasting benefit to his fellow citizens."

## KENTUCKY

**Pediatric Conferences.**—On October 22 Drs. Philip F. Barbour, Louisville, and J. Garland Cherrill, consultant in pediatrics and consultant in surgery for children, respectively, for the state department of health, will conduct a pediatric conference in Corbin with the Whitley County Medical Society and the county health department. The program will include lectures and a clinic. The Muhlenberg County Medical Society will present a meeting on October 24 in Greenville, including a pediatric and obstetric clinic. A pediatric conference will be offered in Pineville, October 29, with Dr. Thomas M. Marks, Lexington, and Dr. Barbour in charge. Dr. Stanley S. Parks, Lexington, will be available as a consultant on obstetric patients. On November 12 a pediatric clinic will be conducted by Dr. Robert B. Warfield, Lexington, and Dr. Barbour in Paintsville, with Dr. A. J. Whitehouse, Lexington, as consultant in obstetric care. These various programs are being held throughout the state under the sponsorship of the county medical societies and the local health departments and under the general supervision of the state medical association and the state department of health.

## MISSOURI

**Health Board Resigns in Protest.** — Resignation of all members of the health board of Cape Girardeau in protest against failure of the city to follow its recommendations for more strict scrutiny of milk distribution and adoption of rules regulating health conditions in restaurants was accepted by the city council on August 2, newspapers report. A complete new board was appointed. Retiring board members included Drs. Carl A. W. Zimmermann, chairman, William F. Oechler, John H. Cochran and Raymond A. Ritter. Members of the new board are Drs. Gustav B. Schulz, Alexander E. Dalton, Hugh V. Ashley and Amos M. Murphy.

**Report of State Cancer Hospital.** — A total of 3,374 patients have been examined in the Ellis Fischel State Cancer Hospital in Columbia from the time it opened in May 1940 through Feb. 28, 1943. There have been 13,225 clinic visits. These patients came from practically every county in the state with the exception of the St. Louis and Kansas City districts. The 931 physicians who sent patients to the hospital make up 48.6 per cent of all the physicians in the state, exclusive of Kansas City and St. Louis. One physician sent 49 patients. The average hospital stay per patient for 1942 was 18.5 days. The cost per patient day was $6.30. About 40 per cent of the proved carcinoma cases and 25 per cent of the surgical pathologic cases were made up of skin lesions. Carcinoma of the rectum was a fairly common lesion, and of 81 consecutive cases 57, or 70 per cent, were resectable. According to a report published in the state medical journal by Dr. Lauren V. Ackerman, medical director and pathologist of the hospital, about 150 cases of carcinoma of the breast are seen yearly and fifty radical mastectomies are being done. Thus far there have been no operative deaths. The distribution of carcinoma at the state cancer hospital does not conform with accepted statistical studies, it was stated. To consider how many patients have true carcinoma, a thousand consecutive cases were analyzed, and malignant disease was present in only 52 per cent. Forty-three per

cent were proved definitely not to have carcinoma and 5 per cent could not be classified. Of the nonmalignant lesions, 341 were located in the uterus, skin, breast, stomach, rectum, penis and sigmoid. According to the state law all patients admitted to the hospital must be indigent, as certified by the patient's local county court, and a diagnosis of carcinoma or precancerous condition must be made by the referring physician from that county. All patients admitted to the hospital with malignant disease are treated from a curative or palliative approach. Patients with advanced disease which cannot be benefited by treatment are not admitted.

## NEBRASKA

**Mid-West Clinical Society.**—The Omaha Mid-West Clinical Society will hold its eleventh annual assembly at the Hotel Paxton, Omaha, October 25-29. Among the out of state speakers will be:

Dr. Harold G. Wolff, New York, Headache Mechanisms.
Dr. Jennings C. Litzenberg, Minneapolis, Management of Occiput Posterior.
Dr. Frank R. Ober, Boston, Infantile Paralysis.
Dr. Raymond W. McNealy, Chicago, Advances in Blood Vessel Surgery.
Dr. Sara M. Jordan, Boston, Functional Diseases and the War.
Dr. Luther Emmett Holt Jr., Baltimore, Unusual Cerebral Disorders in Childhood.
Dr. Sanford R. Gifford, Chicago, Treatment of Some Corneal Diseases.
Dr. Robert L. Sanders, Memphis, Tenn., Complications of Duodenal Ulcer.
Dr. Tom D. Spies, Birmingham, Detailed Methods of Diagnosis and Therapy in Acute Nutritive Failure.
Col. Rexford L. Diveley, M. R. C., The Work of the Rehabilitation Centers in England (tentative).
Dr. Cyrus E. Burford, St. Louis, Present Day Management of Carcinoma of the Prostate.
Major General Norman T. Kirk, surgeon general of the U. S. Army, Amputations (tentative).

There will be symposiums on peripheral vascular diseases, pneumonia and shock and special lecture courses. Thursday evening has been designated "Omaha-Douglas County Medical Society Night" and speakers will include Dr. Eben J. Carey, Milwaukee, on "Medical Education of Today and Its Effect on the Future of Medicine." The session will conclude Friday morning with a panel discussion on "War Medicine and Surgery" with Capt. Henry L. Dollard (MC), U. S. Navy, acting as chairman. Other speakers will be:

Capt. Emil J. Stelter (MC), U. S. Navy, Aviation Medicine and Research.
Comdr. John F. Luten (MC), U. S. Navy, Treatment of War Casualties, Including Shock, Plasma and Sulfonamides.
Lieut. Comdr. Franklin C. Southworth Jr. (MC), U. S. Naval Reserve, Neuropsychiatric Screening of Recruits at a Naval Training Station.
Lieut. Comdr. Charles W. McLaughlin Jr. (MC), U. S. Naval Reserve, Corrective Surgery.
Lieut. Comdr. Joseph M. Picciochi (MC), U. S. Navy, 25,000 Photofluorographs of the Chests of Naval Recruits.

## NEW HAMPSHIRE

**Dr. Mary Atchison Named Acting State Health Officer.**—Dr. Mary M. Atchison, formerly director of the divisions of maternal and child health and crippled children's services, New Hampshire State Board of Health, Concord, and recently acting deputy secretary of the state board, has been appointed acting state health officer. Dr. Atchison fills the vacancy that occurred when Dr. Alfred L. Frechette was granted a leave of absence as secretary of the board to engage in war rehabilitation work under the auspices of the U. S. Public Health Service (THE JOURNAL, July 17, p. 821).

**The Mayo Lectures.**—Capt. Winchell M. Craig (MC), U. S. Naval Reserve, chief surgeon, Naval Hospital, Naval Medical Center, Bethesda, Md., will deliver the W. J. and C. H. Mayo Memorial Lecture at Dartmouth Medical School, Hanover, November 5. The title of his address will be "Warriors Against Disease." The lecture was established in 1942 by Dr. and Mrs. Waltman Walters, Rochester, Minn., as "a stimulating factor in interesting men in medicine and surgery and, particularly, to call attention to the accomplishments of Drs. W. J. and C. H. Mayo in these fields."

## NEW JERSEY

**Schireson's License Restored.**—The New Jersey state court of pardons and appeals set aside on September 24 the action of the state board of medical examiners in revoking the license of Dr. Henry J. Schireson, Merchantville, plastic surgeon, according to the New York *Times*. The errors court, in an opinion written by Chief Justice Thomas J. Brogan, held that although Schireson at the time his license was revoked, April 15, 1942, was serving a federal penitentiary sentence for perjury, false swearing and concealing assets in federal bankruptcy proceedings, the physician had not been convicted of a crime, the report stated. Schireson was once involved in a notorious damage suit in which he was ordered to pay the complainant $40,000. Since then his licenses to practice medicine in various states have been revoked.

## NEW YORK

**New Building at Lederle.**—A five story and basement reinforced concrete and brick factory and laboratory building has been started at the Lederle Laboratories, Inc., Pearl River. The expansion is in accordance with recently approved priorities from the War Production Board to meet the required need of penicillin.

**Personal.**—Dr. William T. Shanahan has retired as medical superintendent of the Craig Colony, Sonyea, effective October 1. He plans to live in Eggertsville. Dr. Shanahan has been medical superintendent for thirty-two of the forty-seven years with which he has been connected with Craig Colony, an institution for the epileptic.

### New York City

**Tuberculosis Package Library.**—The Queensboro Tuberculosis and Health Association launched a library health package service recently to supply, free of charge, new books, pamphlets and research studies on tuberculosis to libraries throughout the borough.

**Louis Livingston Seaman Fund.**—The New York Academy of Medicine announced that the Louis Livingston Seaman Fund of $1,000 is now available. Applications will be received either from institutions or from individuals up to November 1. The fund will be expended only in grants in aid for investigation or scholarships for research in bacteriology or sanitary science and may be made for securing of technical help, aid in publishing original work and the purchase of necessary books or apparatus. The fund was made possible by the terms of the will of the late Dr. Louis Livingston Seaman. Additional information may be obtained from Dr. Wilson G. Smillie, chairman of the fund, 1300 York Avenue.

**Grant for Undergraduate Psychiatric Education.**—The Commonwealth Fund has awarded a six year grant to the Long Island College of Medicine, Brooklyn, for the development of undergraduate psychiatric education, beginning with the sum of $20,450 toward the current budget. The aims of the projected program are to train the medical student to understand and recognize the personal and environmental factors that often contribute to ill health, both physical and mental, the impact of somatic illness on personality, and the diagnosis and treatment of psychologic problems long before these grow into fully developed psychiatric disorders as one of the responsibilities of physicians in the mental hygiene area of public health and hygiene.

**Opinion Reverses Revocation of Compensation License.**—In a decision handed down on September 8 Supreme Court Justice Carroll G. Walter voided an action of the New York State Industrial Commission in revoking the authority of Dr. Leo S. Sacharoff to treat workmen's compensation cases. Dr. Sacharoff lost his license to care for this work on August 11 by order of the state labor department because of fee splitting and other misconduct (THE JOURNAL, September 4, p. 46). The physician's right to treat such cases was rescinded as a result of the Moreland commission's investigation into the administration of the workmen's compensation act. In annulling the revocation action Justice Walter held that the commissioner had no legal right to hold a hearing and that the charges of professional misconduct first should have been heard by the county medical society having jurisdiction, according to the New York *Times*. In the event that the medical body sustained the charges, Justice Walter pointed out in his decision, the industrial commissioner might then act to revoke the physician's right to administer to compensation cases.

## NORTH CAROLINA

**Dr. Ferguson Named Professor of Physiology.**—Dr. John H. Ferguson, assistant professor of pharmacology, University of Michigan Medical School, Ann Arbor, has been appointed professor and head of the department of physiology at the University of North Carolina School of Medicine, Chapel Hill. Dr. Ferguson graduated at Harvard Medical School, Boston, in 1928.

**New Building for Health Unit.**—A new two story building has been erected in Wilmington for the consolidated board of health of New Hanover County and the city of Wilmington. Most of the lower floor is given to the clinics, examination and treatment rooms and office for the malaria control staff, and the fluoroscope room. The second floor is devoted to

administrative facilities. The general public health laboratory and the venereal disease laboratory will remain in the court house. The unit was constructed by the Federal Works Administration, which leased the lot and constructed the building at a cost of about $30,000. Ultimately the lease will be terminated and the lot and building will be turned over to the county.

## OHIO

**Industrial Funds Distributed Reach New High.**—The state industrial commission disbursed $4,243,069.09 for medical services to injured Ohio workers during 1942, according to a recent report. The figure, which established a new record for this expenditure, includes a relatively small amount for essential dental services. Other expenditures during the year included $1,760,898.69 for hospital care and nursing, $133,104.41 for funeral expenses and $86,644.34 for court costs, a total of $6,223,733.53. These amounts include payments covering injuries to private and public employees as well as similar costs on occupational disease claims and are in addition to death awards and compensation to injured employees. Comparative figures for 1941 were $3,322,792.06 for medical services, $1,258,095.36 for hospital care and nursing, $122,290.05 for funeral expenses and $73,998.89 for court costs, a total of $4,777,177.26. The number of claims filed during 1942 was 320,793, also a record for the thirty-one year history of the Workmen's Compensation Fund. There were 286,010 claims filed in 1941, the previous peak year. The total for 1932 was 130,099. "Medical only" claims, involving payment for physicians' services but no compensation to the claimant for loss of time, numbered 256,600 in 1942, or 80 per cent of all claims filed, compared with 79.5 per cent in 1941. Average expense of "medical only" claims decreased from $8.03 in 1941 to $7.69 in 1942.

## OKLAHOMA

**Thirteenth Annual Clinic Society Conference.**—The Oklahoma City Clinical Society will hold its thirteenth annual conference at the Biltmore Hotel, Oklahoma City, October 18-21. The guest speakers will be:

Dr. Louis E. Phaneuf, Boston, Evolution, Indications and Contraindications of Cesarean Section.
Dr. Abraham H. Aaron, Buffalo, The Management of Peptic Ulcer from the Standpoint of the Active Practitioner.
Dr. Charles T. Way, Cleveland, Clinical Problems Involving Water, Protein and Solute Replacement.
Dr. Grayson L. Carroll, St. Louis, The Clinical Management of Pyuria.
Dr. Robert D. Schrock, Omaha, Fractures at the Knee Joint.
Dr. Vilray P. Blair, St. Louis, The Importance of Proper Early Treatment of Face Injuries.
Dr. John A. Toomey, Cleveland, Chemotherapy in Acute Infectious and Contagious Diseases.
Dr. Leroy A. Calkins, Kansas City, Mo., I Haven't Been the Same Since Mary Was Born (a diagnostic problem).
Dr. Theodore J. Dimitry, New Orleans, The Modern Trend in the Treatment of Eye Diseases.
Dr. Thomas G. Orr, Kansas City, Mo., Analysis of Gallbladder Cases.
Dr. George B. Eusterman, Rochester, Minn., "When Johnnie Comes Marching Home" (diagnostic and therapeutic problems facing the practitioner and how to meet them).
Dr. Harry E. Mock, Chicago, Skull Fractures and Brain Injuries (a review of the management of 7,031 cases treated throughout the United States).
Dr. Louis A. Buie, Rochester, Minn., Lesion of the Terminal Portion of the Colon.
Col. Franklin G. Ebaugh, M. C., A. U. S., Basic Neuropsychiatric Induction Examination Problem (How the General Medical Profession Can Help).
Dr. W. Likely Simpson, Memphis, Tenn., Diagnosis and Treatment of Sinusitis.
Dr. Clinton W. Lane, St. Louis, Contact Dermatitis with Particular Reference to Occupational Dermatitis.

The program will also include round table luncheons and banquets.

## OREGON

**Life Members of State Society.**—At a meeting of the council of the Oregon State Medical Society, August 14, life membership was voted to Drs. Charles T. Sweeney, Medford; George Norman Pease, Portland; William T. Johnson, Corvallis, and the late Wilson Johnston, Portland.

**Dr. Weeks Observes Ninetieth Anniversary.**—Dr. John E. Weeks, professor emeritus of ophthalmology, New York University College of Medicine, New York, celebrated his ninetieth birthday recently. Dr. Weeks was for many years professor of ophthalmology at University and Bellevue Hospital Medical College, New York, becoming emeritus professor in 1920. He was chairman of the Section on Ophthalmology of the American Medical Association in 1902.

## SOUTH CAROLINA

**Dr. Routh Resigns from State Board.**—Dr. Foster M. Routh, Columbia, for many years a member of the executive committee of the state board of health and chairman in 1935, resigned as a member of the board on August 18 because of ill health. Dr. Robert B. Durham, Columbia, has been named to succeed Dr. Routh, who will continue his work as resident physician at the University of South Carolina, Columbia. Dr. Routh graduated at the Medical College of the State of South Carolina, Charleston, in 1910.

## TENNESSEE

**New State Health Officer.**—Dr. Robert H. Hutcheson, Nashville, assistant commissioner and one time superintendent of the Williamson County Health Unit, has been appointed state commissioner of public health. He succeeds Dr. Wilson C. Williams, Nashville, who accepted a commission as lieutenant colonel in the Medical Corps of the Army and who has been ordered to active duty. Dr. Hutcheson graduated at the University of Tennessee College of Medicine, Memphis, in 1930.

## UTAH

**State Medical Election.**—Dr. Ezekiel R. Dumke, Ogden, was named president-elect of the Utah State Medical Association at its annual session in Salt Lake City and Dr. James P. Kerby, Salt Lake City, was inducted into the presidency. Other officers include Drs. Wilford Woolf, Provo, LaVille H. Merrill, Spring Canyon, and Mildred N. Nelson, Salt Lake City, vice presidents; Dr. David G. Edmunds, Salt Lake City, secretary, and Dr. Edward S. Pomeroy, Salt Lake City, treasurer. The next annual session will be held in Salt Lake City sometime in August 1944.

## WISCONSIN

**Physicians Honored.**—The Waukesha County Medical Society held a banquet recently at the Draper Hall, Oconomowoc, to honor Drs. Michael R. Wilkinson, Oconomowoc, Byron M. Caples, Waukesha, and Francis J. Donnelly, North Lake, in recognition of their completion of fifty years in the practice of medicine; each was awarded an honorary life membership in the county society.

**Will Provides for Hospital.**—The estate of the late Dr. William H. Finney will eventually be available for the erection and maintenance of the William Finney Memorial Hospital in Clintonville under the provisions of the physician's will filed on July 30. The estate is estimated to be about $400,000 and will be divided among the beneficiaries during their lifetime. On their deaths one half is to go to the city of Clintonville to build and equip a modern hospital to bear his name.

## GENERAL

**Examination in Otolaryngology.**—The American Board of Otolaryngology announces that it will conduct an examination in Los Angeles, February 2-5, provided fifty applicants are accepted.

**New Executive Director of the Russian War Relief.**—Fred Myers, public relations director of Russian War Relief, New York, since its inception in 1941, has been appointed executive director to succeed Arch Mandel, who resigned to join Community Chest and Councils, Inc.

**Meeting of Industrial Hygiene Foundation.**—The eighth annual meeting of the Industrial Hygiene Foundation will be held at the Mellon Institute, Pittsburgh, November 10-11. At a meeting of the board of trustees on August 25 it was decided to hold the meeting as a help in maintaining healthful conditions in war plants, which in turn helps maintain manpower.

**Casselberry Award.**—The American Laryngological Association announced that a sum of money has accrued from the Casselberry Fund to insure a prize being offered in 1944 for original investigation in the art and science of laryngology or rhinology. Theses must reach the secretary, Dr. Arthur W. Proetz, 1010 Beaumont Building, St. Louis 8, before March 1, 1944.

**Examinations for Medical Technologists.**—The Registry of Medical Technologists of the American Society of Clinical Pathologists announces that examinations of applicants for registration will be conducted in various parts of the United States and Canada on October 29. Additional information may be obtained from Dr. Lall G. Montgomery, chairman of the Board of Registry of Medical Technologists, Ball Memorial Hospital, Muncie, Ind.

**Society News.**—The National Association for Nursery Education will hold its tenth biennial meeting at the Hotel Statler in Boston, October 22-25. There will be a conference on "The Community Serves the Child in War and Peace" and one session on "The World Picture and the Implications for Education." Other sessions will consist of study groups which will

discuss child development problems based on actual case histories of various communities. Dura-Louise Cockrell, state social security commission, Jefferson City, Mo., is the secretary of the National Association for Nursery Education.

**Brazilian Physician Lectures on Tropical Medicine.**—At the invitation of the Pan American Sanitary Bureau, Dr. Olympio da Fonseca Jr., medical director for Brazil for E. R. Squibb and Sons Inter-American Corporation, has arrived in the United States for an extensive lecture tour before the faculties and students of medical schools throughout the country, discussing tropical medicine with special emphasis on malaria, African sleeping sickness, amebic dysentery and ringworm infection. Dr. da Fonseca is a professor at the National School of Medicine of the University of Brazil and is connected with the Medical Center of Ceara and the department of health of that state.

**Special Society Elections.**—Dr. Fuller Albright, Boston, is president of the American Society for Clinical Investigation for 1943-1944, and Dr. Wesley W. Spink, Minneapolis, is secretary.——Dr. H. Marshall Taylor, Jacksonville, Fla., is president of the American Laryngological, Rhinological and Otological Society. The society did not have an annual meeting this year, and the council promoted Dr. Taylor from president-elect to president. He succeeds Dr. James G. Dwyer, New York, who resigned as president. Vice presidents appointed for the ensuing year are Drs. Westley M. Hunt, New York; William C. Warren Jr., Atlanta, Ga.; Fred W. Dixon, Cleveland, and Simon Jesberg, Los Angeles.

**Profession-Industry Follow-Up Conference.**—The second Profession-Industry Follow-Up on the National Conference on Planning for War and Postwar Medical Services was held at the Waldorf-Astoria, New York, October 4, under the auspices of the National Physicians Committee for the Extention of Medical Service. Among the speakers on the program were Dr. Roger I. Lee, Boston, on "Medicine's Position and Policy," Raymond Moley, Ph.D., New York, "The Cult of the Uncommon Man," and Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, "Medical Planning and Progress." Dr. Edward H. Cary, Dallas, Texas, was chairman at the meeting, at which the financial report and reports covering the educational efforts and the profession-industry cooperation were reviewed.

**Remington Award Goes to Dr. Fischelis.**—Robert P. Fischelis, Ph.M., Trenton, N. J., chairman of the council of the American Pharmaceutical Association, has been awarded the 1943 Remington Medal, conferred by the New York Branch of the American Pharmaceutical Association. Dr. Fischelis, who is secretary and chief chemist of the Board of Pharmacy of the State of New Jersey and chief of the chemicals, drugs and health supplies branch of the Office of Civilian Requirements of the War Production Board, was presented with the medal for his many contributions to the advancement of pharmacy, including his literary, scientific and organizational activities. He has recently been reappointed as the pharmacist member of the state board of health of New Jersey for a term of four years. The Remington Medal is awarded annually "to the man or woman who has done most for American pharmacy during the preceding year or during a longer period of outstanding activity and of fruitful achievement."

**Pacific Coast Society of Obstetrics and Gynecology.**—The annual meeting of the Pacific Coast Society of Obstetrics and Gynecology will be held in San Francisco, November 4-5, under the presidency of Dr. C. Frederic Fluhmann, San Francisco. Among the speakers will be:

Dr. Howard C. Stearns, Portland, Ore., Extraperitoneal Cesarean Section: Analysis of a Short Series.
Dr. Ernest W. Page, Berkeley, Calif., The Metabolism of Histidine During Pregnancy.
Dr. Karl L. Schaupp, San Francisco, Unusual Case of Abdominal Pregnancy.
Dr. Goodrich C. Schauffler, Portland, Women in Heavy War Industries: Gynecologic and Obstetric Aspects.
Dr. Albert V. Pettit, San Francisco, The Closure of Lower Abdominal Incisions.
Dr. Frederic M. Loomis, Sausalito, Calif., De Senectute: "The Good That We Would, We Do Not; the Evil That We Would Not, That We do."
Carl G. Hartman, Ph.D., Baltimore, Securing Monkey and Human Embryos.

Another feature of the meeting will be a symposium on "Erythroblastosis Fetalis." Dr. Herbert M. Evans, Berkeley, and Charles H. Danforth, Ph.D., Stanford University, will discuss "Story of Implantation in Primates."

**Association of American Medical Colleges.**—The fifty-fourth annual meeting of the Association of American Medical Colleges will be held at the Hotel Statler, Cleveland, October 25-27, under the presidency of Dr. Waller S. Leathers, dean of the Vanderbilt University School of Medicine, Nashville. Speakers on the program will include:

Dr. Henry E. Meleney, New York, Tropical Medicine Fellowships of the John and Mary R. Markle Foundation.
Brig. Gen. George F. Lull, and Col. Francis M. Fitts, M. C., U. S. Army, The Army Specialized Training Program.
Comdr. Bartholomew W. Hogan (MC), U. S. Navy, The Navy V 12 Program.
Dr. Victor E. Johnson, Secretary, Council on Medical Education and Hospitals, American Medical Association, Chicago, Effect of the Accelerated Program of Medical Schools on the Curriculum, Faculty and Students.
Dr. Willard C. Rappleye, New York, Postwar Planning for Medical Education.
Dr. Lester J. Evans, New York, The Place of the Small Community Hospital in Postwar Medical Education.
Dr. Allan Gregg, New York, Can Excellence be Learned?
M. B. Harrower-Erickson, Madison, Wis., The Rorschach Test.
Philip A. Shaffer, Ph.D., St. Louis, A Recipe for a Medical School.
Dr. Carey P. McCord, Detroit, Some Aspects of Medical Education in Industrial Health Conservation.
Dr. Joseph T. Wearn, Cleveland, Present Methods of Medical Teaching.
Dr. Carl J. Wiggers, Cleveland, Correlation of Physiology Instruction with War Problems.

**Aero Medical Association Meeting.**—The fifteenth annual meeting of the Aero Medical Association of the United States will be held in the Netherland Plaza Hotel, Cincinnati, October 26-27. Among the speakers will be:

Dr. Albert J. Herbolsheimer, Washington, D. C., The Role of Extraocular Muscles in the Aviation Physical Examination.
Dr. William J. Holmes, Honolulu, Hawaii, Night Vision, Fundamental Considerations.
Dr. Whitman C. McConnell and Dr. Whitman H. McConnell, St. Petersburg, Fla., Neuropsychiatric Aspects of the Civilian Pilot Examination.
Dr. Edgar E. Poos, Detroit, Allergy of the Upper Respiratory Tract.
Drs. Ralph Bretney Miller, Washington, D. C., Emerson Day, Baltimore, LeMoyne White, Walpole, N. H., and John M. Baldwin, New York, Medical Problems in an Overseas Air Transport Service.
Lieut. Comdr. Marion M. Kalez (MC), U. S. Naval Reserve, Observations on the Odd and Strange in the South Pacific.
Brig. Gen. Eugen I. G. Reinartz, M. C., U. S. Army, Observations on Aviation Medicine in the European and African Zones.
Lieut. Col. Richard L. Meiling, M. R. C., Air Evacuation of Casualties.
Dr. Alberto Hurtado, Lima, Peru, Comparative Studies Among Flight Personnel and Residents in the Peruvian Andes.
Major Herman S. Wigodsky, M. R. C., Army Air Forces Altitude Training Program.
Lieut. Comdr. Earle E. Metcalfe (MC), U. S. Navy, Navy Low Pressure Chamber Indoctrinal Program.
Lieut. Comdr. John W. Jenkins, H-V (S), U. S. Naval Reserve, Prediction of Flight Training Performance by Biographic Data.
Major Arthur B. Welton, A. C., A. U. S., Selection of Pilots by Means of Psychometric Tests.
Lieut. Comdr. Ashton Graybiel (MC), U. S. Naval Reserve, Fatigue as a Problem in Aviation Training.
Squadron Leader K. Evelyn, R. C. A. F., Ottawa, Ont., Night Vision.
Capt. George M. Hass, M. C., A. U. S., Aircraft Injuries.
Major F. G. Hall, A. C., A. U. S., and Alice Brues, Ph.D., Dayton, Ohio, Simultaneous Measurements of Pulse Rate, Pulmonary Ventilation and Inspiratory Pressure.
Comdr. Chalmers L. Gemmill (MC), U. S. Naval Reserve, The Testing of Oxygen Equipment.
Col. Gustave E. Ledfors, M. C., U. S. Army, Progressive Changes in Medical Field Equipment.
Capt. Bertram Groesbeck Jr. (MC), U. S. Navy, Modern Trends in the Teaching of Aviation Medicine.
Lieut. Comdr. Herman J. Sternstein (MC), U. S. Naval Reserve, The Effect of Nasal Ventilation on Tubal Equalizing Efficiency in Flying Personnel.
Air Commodore J. W. Tice, R. C. A. F., Ottawa, Ont., Current Medical Developments in the Royal Air Forces.
Capt. John C. Adams (MC), U. S. Navy, Developments in Naval Aviation Medicine.
Brig. Gen. David N. W. Grant, M. C., U. S. Army, Medical Service with the Army Air Forces.
Dr. William R. Stovall, Washington, D. C., Trends in Civil Aviation Medicine.
Lieut. Albert Damon, A. C., A. U. S. The Importance of Human Sizing Standards in Aviation.
Capt. Alvin M. Cahan, M. C., A. U. S., The Improved Methods of Resuscitation.
Lieut. Col. William R. Lovelace II, M. R. C., Aviation Medical Research in Aircraft at High Altitudes.

Another feature of the meeting will be a civil aeronautics medical forum, Wednesday, with Dr. Stovall in charge.

## *Government Services*

### Dr. Wilder Resigns from Food Administration

Dr. Russell M. Wilder has resigned as chief of the civilian food requirements branch of the Food Distribution Administration to return to his activities at the Mayo Clinic, Rochester, Minn. He will continue to serve as medical adviser to the administration. According to the Washington *Post*, September 19, Norman Leon Gold, Silver Spring, Md., assistant to the administrator of agricultural marketing administration, U. S. Department of Agriculture, will become acting chief of the branch.

# Foreign Letters

## LONDON

*(From Our Regular Correspondent)*

Aug. 20, 1943.

### Diphtheria Problems

The Fever Group of the Society of Medical Officers of Health has issued an important memorandum on diphtheria problems. Artificial immunization has much reduced the incidence of the disease and minimized its severity. But the variation in the classic signs has increased difficulty in diagnosis, and without evidence of complete immunization, as shown by a negative Schick test, immunity cannot be safely assumed. Further, diphtheria may occur, though rarely, in a Schick negative person. There is a tendency to place undue reliance on the swab examination. The bacteriologist cannot distinguish between active diphtheria and the carrier state. Doubtful cases must be examined for hemolytic streptococci and Vincent's organisms. Antitoxin must be given at the earliest possible moment, normally in a hospital, as a maximum dose is advisable rather than a series of smaller ones. Only when there has been delay or is likely to be delay should the physician give antitoxin. Antitoxin need not be withheld for fear of severe reactions. The modern protein digested concentrated product rarely gives rise to serum sickness or related phenomena.

In case of doubt continuous observation is necessary and the patient should be sent to a hospital. The procedure today in many hospitals is as follows: 1. When delay in administering antitoxin would be dangerous it should be given immediately before any bacteriologic investigation. 2. When delay of six hours would not be dangerous the Schick test should be performed, swabs taken and antitoxin given six hours later. 3. When delay of one day or more would not be dangerous, antitoxin should be deferred until the results are known. In no case should reliance be placed on the swab alone; every suspected patient when first seen must either receive antitoxin and have the throat or nose swabbed or must be given the Schick test and have the throat or nose swabbed. When there is doubt, antitoxin should be given.

A person whose throat or nose is swabbed because of contact with a diphtheria patient but who has no symptoms must not be classed as having diphtheria, notified or sent to a hospital merely because of a positive finding. Routine swabbing of contacts, except in special circumstances, such as institutional outbreaks, is to be deprecated and should at any rate be restricted to those showing an unhealthy condition of the nasal or pharyngeal mucosa. The waste of time, effort and material is not justified by the occasional discovery of a healthy carrier.

### Blind Factory Workers

The Ministry of Labor and National Service has a list of more than eighty occupations in which blind persons have been placed. During the past twelve months over 700 blind men and women have been given jobs formerly done by sighted workers. It is claimed for the blind that they often show unusual powers of concentration and have supersensitive hearing and touch. Keenness of hearing is known to enable a blind operative to detect a blunted cutter or a slight irregularity in the running of a machine which another person would miss. For the most part the blind are given simple process work for which little, if any, preliminary training is needed. But a good many have proved capable of doing intricate assembly work.

What is the accident risk among blind workers? The general experience of blind welfare officers is that the blind factory worker is more than ordinarily careful and that the risk of accident is negligible. The chief insurance companies do not refuse blind persons, nor do they increase the premium for a blind worker provided the employer can assure them that the work is within the worker's capacity.

On the staff of the Ministry of Labor there are eleven blind shorthand typists and fifty blind telephonists. Many men blinded in the last war are still capable of work. Some months ago the works manager of a London factory inquired urgently of the employment exchange for four men of a particular type. "I must have some one," he said, "for it is an important job though simple. I could do it with my eyes shut." There was no one on the register and the exchange manager suggested that he might engage some blind men. The trial was so successful that a week later he engaged four more.

### A New "Ophthalmic" Camera

Wing Commander Harold Pearce, director of photography at the Royal Canadian Force headquarterts, has been elected a fellow of the Royal Photographic Society of Great Britain for his part in the invention of a new "ophthalmic" camera developed by that force for studying vitamin deficiencies revealed by the eye. As a result of studies with the camera the medical officers of the force have shown that airmen who finish flights rubbing their eyes, which feel tired and watery, often suffer from a lack of vitamin $B_2$, or riboflavin. In order to inspect men's eyes and obtain a permanent record of examinations, a special camera was designed by Wing Commander Pearce and Flying Officer M. J. Sym, an authority on microscopic camera work at the University of Manitoba, who worked out the technical details for a 2,000,000 watt bulb which flashes for a split second into the eye camera.

### British Medical Aid for China

The British Red Cross Society sent last year a hospital unit of twenty-one persons—doctors and nurses—for service in China. It was under the direction of Dr. W. S. Flowers and established a base hospital at Changsha, Hunan, where sick and wounded, both civilian and military, are being treated and excellent work is being done. In the medical press Lord Horder states that an appeal has been received by the War Organization of the British Red Cross for reinforcements. It is stated to be especially desirable that applicants should have a knowledge of the Chinese language or a background of Chinese experience. Further particulars may be obtained from Dr. H. Gordon Thompson, War Organization of the British Red Cross, 14 Grosvenor Crescent, London, S.W. 1.

### C. J. S. Thompson, Medical Historian and Curator

The death of C. J. S. Thompson, Ph.D., has removed an important figure from the medical world, though he was not a member of the medical profession. Born in 1862, he devoted his early days to the study and practice of chemistry and pharmacy with special attention to history. In 1900 he was appointed curator of the projected Wellcome Historical Medical Museum. Until his retirement in 1926 he threw all his energy into gathering and organizing that unrivaled collection. In the course of his work he traveled extensively in Europe. In 1927 the Royal College of Surgeons appointed him honorary curator of the historical section of its museum. He worked at this until the collection was almost completely destroyed by German bombing in 1941. Fortunately he had then completed his great work "The History and Evolution of Surgical Instruments," which was published last year in New York and which is a permanent record of some of the most important exhibits of the museum. His lifelong study of toxicology gave rise to "Poisons and Poisoners," a standard reference work on the history of poisoning. Other important works from his pen were "The Art of the Apothecary" (1929) and "The Secrets of Magic" (1927).

## BUENOS AIRES

*(From Our Regular Correspondent)*

Sept. 1, 1943.

### Mortality in Laryngectomy

Drs. Robert C. Ferrari and Edgar Flemming recently read an article before the Argentina Academy of Surgery on the surgical results of laryngectomy in 193 cases which were classified in four different groups on the basis of mortality rates: 1. Endolaryngeal cancer with neither tracheal obstruction nor complications and associated diseases in young and strong patients. Twenty-four cases were included in this group, and there was no surgical mortality. 2. Endolaryngeal cancer with tracheal obstruction, with or without previous tracheotomy, including cancer of the epiglottis and cancer with involvement of the pharyngeal wall. Patients in this group were between 50 and 60 years of age, in good general condition. One hundred and ten cases were included in this category. The mortality was 3.7 per cent. 3. Cancer of the epiglottis with involvement of the tongue and laryngeal cancer with destruction of the larynx and involvement of the surrounding soft tissues. Moderate doses of x-rays were given. The patients were over 60 years of age, in poor general condition. Forty-nine patients were classified in this group. Twelve patients died. 4. Cancer heavily irradiated, including laryngeal carcinoma in patients with associated diseases such as diabetes, nephrosclerosis and chronic pulmonary or cardiac conditions. Nine cases fell in this group. The surgical mortality was 45 per cent.

### Public Health in Uruguay

Dr. Mussio Fournier, minister of public health in Uruguay, has published an extensive study on the activities of this service in the last four years. Several departments were considerably improved. The development of the Center of Prophylaxis and Study of Hydatid Disease deserves special mention because of the importance of this disease in Uruguay. The intensification of the antituberculosis campaign has led to an increase of 130 per cent in the number of beds reserved for tuberculous patients (from 1,555 beds in 1937 to 2,437 beds in 1942). The newly created service for mass radiologic chest survey has examined 50,000 persons in two years. Eight new tuberculosis sanatoriums and several outpatient clinics were established. There are large new pavilions for patients with mental disease with a capacity of 1,000 beds in the Colonia Bernardo Etchepare. The crusade against trachoma is intensified throughout the country. The Department of Industrial Hygiene, the Instituto de Orotopedia y Traumatología, the Centro de Protección al Cardíaco and four polyclinics of mental hygiene were also established. A total of 7,500,000 pesos was spent in these improvements and new departments. The Department of Public Health had a total of 12,777 beds available in 1942. The Vital Statistics Department of Public Health was reorganized and modernized. A new Department of Public Help to the Poor was recently created; it is mostly concerned with carrying on investigations in order that the poor may receive necessary medical care. The Dorrego laboratory was also created recently for the preparation of drugs for the hospitals of the country at moderate cost.

### Allergy

Drs. Guido Ruiz Moreno, Miguel A. Solari and Alois A. Bachmann studied 733 clinical reports of patients who were cared for in the Instituto de Investigaciones Físicas Aplicadas a la Patología Humana, a department of the National Academy of Medicine of Buenos Aires. The most frequent allergic syndromes were asthma (431 cases), rhinopathies (360 cases), and urticaria (41 cases). The best therapeutic results were obtained in allergic rhinopathies; 69.5 per cent of allergic rhinopathies and 62.1 per cent of allergic asthma were cured. The specific therapy failed in 1.8 per cent of the cases of rhinopathy and in 4.5 per cent of those of asthma. There were 62.9 per cent multiple sensitivities and 37.1 per cent single sensitivities. Cutaneous sensitivity was not an index of clinical sensitivity. The greatest frequency of the latter is that which is produced by inhaled substances: 50 per cent. Food is the cause of reaction in 29.8 per cent of the cases, pollen in 11.7 per cent and bacteria and mushrooms in 8.5 per cent. House dust and feather dust were the causes in a large number of instances. Streptococci and staphylococci were the cause in about the same number of instances. Aspergillus in the group of mushroom sensibilities and Ambrosia tenuifolia in that of pollens followed, but the gramineous plants were the most frequent in their groups. Allergenic foods in order of frequency were milk, eggs, wheat, fish and pork. It was also found that peas, lentils, rice and beef have allergenic properties. Heredity appeared to be a factor in 69.1 per cent of the cases. Rhinopathies complicated by asthma were observed in 51.9 per cent of the cases. Asthma occurred in about the same number of women as in men. Rhinopathies, urticaria, eczema, headache and conjunctival diseases occurred more frequently in women than in men. Plurisyndromal allergy was rare. Gastrointestinal syndromes were frequently observed in men. The allergic syndromes appeared most often between the ages of 20 and 29 years and less frequently in these under 9 years.

### New Medical Journals

*Revista de la Asociación Argentina de Dietología* is the name of a new medical journal which has recently appeared here. It is the organ of the Instituto Nacional de la Nutrición, Buenos Aires. Dr. Pedro Escudero, head of the institute, is the editor. The first issue, of 84 pages, contains articles on determination of the effect of potassium bromate on the content of thiamine (vitamin $B_1$) in bread, staphylococci as cause of food poisoning, food value of araucaria cones, postwar formulas for feeding children, chemical constitution and vitamins in dehydrated eggs, and chemical constitution of food prepared in Argentina (according to results of analysis carried on in the Instituto Nacional de la Nutrición).

*Revista de Psicoanálisis* is the official organ of the Argentina Association of Psychoanalysis, which is a branch of the International Association of Psychoanalysis. Its purpose is to make available in Spanish the foreign psychoanalytic literature. The editorial staff includes Drs. C. E. Carcamo, G. F. Hardoy, A. Garma, M. Langer, E. P. Riviere and A. Rascovsky. The publication has the support of the Francisco Muñoz Foundation.

### Pan American Week on Neuropsychiatry

The Pan American Neuropsychiatric Week, postponed from 1942 to this year, will be held in the Faculty of Medicine of Buenos Aires, November 7 to 13. Dr. Nerio Rojas will preside. The following physicians have been appointed as official speakers: Drs. Arturo Vivado of Santiago, Gonzalo Bosch of Buenos Aires, Honorio Delgado of Lima, Osvaldo Loudet of Buenos Aires, A. Austregesilo and Fortes Ary Borges of Rio de Janeiro, Vicente Dimitri of Buenos Aires, Camilo Paysse of Montevideo, Jose Belbey of Buenos Aires, Samuel Ramírez Moreno of Mexico, Nerio Rojas of Buenos Aires, Julio Endara of Quito and A. C. Pacheco e Silva of São Paulo. The following official topics will be discussed: "Presenile Psychoses," "Abnormal Personality," "Nonsuppurated Acute Encephalitis," "Conceptions on Schizophrenia," "Psychopathology of Hunger in Legal Medicine" and "Neuropsychiatry of Infections in Latin America."

### Brief Items

The Sociedad Argentina dc Historia le la Medicina honored the memory of Vesalio on the occasion of the fourth centenary since his famous investigations.

# Deaths

**James Franklin Allen** ✠ Pittsburgh; Howard University College of Medicine, Washington, D. C., 1902; University of Pennsylvania Department of Medicine, Philadelphia, 1903; aged 70; died in the Allegheny General Hospital, July 27, of carcinoma of the stomach.

**Thomas D. Armistead,** Roanoke, Va.; Medical College of Virginia, Richmond, 1898; member of the Medical Society of Virginia; formerly city physician and coroner; took part in the establishment of the Burrell Memorial Hospital, where for many years he was on the advisory board; served on the staff and for many years a member of the board of the Roanoke Hospital; aged 69; died, August 6, of carcinoma.

**Clarence Edmund Bair,** Braddock, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1900; aged 71; died, August 3, of valvular heart disease.

**Christo Petroff Balabanoff,** Tacoma, Wash.; University of the City of New York Medical Department, 1888; aged 84; died, August 6.

**Margaret Banta,** Los Angeles; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1903; aged 76; died, July 20, of uremia pyonephrosis, cystitis and pernicious anemia.

**George Richard Beddow,** Pine Grove, Pa.; Temple University School of Medicine, Philadelphia, 1934; member of the Medical Society of the State of Pennsylvania; served for many years as deputy coroner of Pine Grove; aged 35; on the associate staff of the Pottsville Hospital, where he died, August 10, of hypertensive cardiorenal disease.

**Charles Edwin Beecher** ✠ Knoxville, Ill.; Northwestern University Medical School, Chicago, 1905; served on the staffs of the Cottage Hospital and St. Mary's Hospital, Galesburg; aged 63; died, July 14, of streptococcic sepsis.

**Jesse Wilmington Bell** ✠ Walhalla, S. C.; Bellevue Hospital Medical College, New York, 1892; surgeon for the Southern Railroad; aged 76; died, July 14, of heart disease.

**Sherman Grant Berry,** San Diego, Calif.; Marion-Sims College of Medicine, St. Louis, 1893; aged 78; died, July 17.

**Hugo Edward Betz,** St. Joseph, Mich.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1896; member of the Illinois State Medical Society; at one time trustee of the Chicago Medical Society; formerly professor of dermatology at his alma mater; superintendent of the Iroquois Memorial Hospital, Chicago, from 1915 to 1924 and formerly on the staff of the Cook County Hospital, Chicago; aged 81; died in Berrien Springs, July 29, of thromboangiitis obliterans.

**John Philip Boland,** Chicago; Rush Medical College, Chicago, 1928; commissioned a captain in the medical corps, Army of the United States, June 22, 1942, relieved from active duty Jan. 2, 1943 and dishonorably discharged, Jan. 19, 1943; aged 41; died, January 18, of an overdose of barbiturate poisoning.

**Edwin C. Bollinger,** Toledo, Ohio; Chicago Physio-Medical College, 1894; served on the staff of the Women's and Children's Hospital; aged 72; died, July 27, of heart disease.

**Arthur Stout Boyett,** Buena Vista, Ga.; University of Nashville (Tenn.) Medical Department, 1894; Vanderbilt University School of Medicine, Nashville, 1894; mayor of Buena Vista; served as state representative and as chairman of the board of county commissioners; aged 73; died, July 30.

**Raleigh Virgil Butler,** Minneapolis; University of Minnesota Medical School, Minneapolis, 1937; aged 39; died in July.

**Herbert William Case,** East Tawas, Mich.; Michigan College of Medicine and Surgery, Detroit, 1904; aged 60; died, July 15, of lobar pneumonia.

**Charles Ellis Clark,** Baltimore; the Hahnemann Medical College and Hospital, Chicago, 1912; served during World War I; formerly on the staff of the Hahnemann Hospital; aged 63; died, July 25, of heart disease.

**Fred William Compton,** Olivehurst, Calif.; University Medical College of Kansas City, Mo., 1888; aged 80; died in Marysville, June 10, of coronary occlusion and coronary sclerosis.

**Thomas John Connor** ✠ Arlington, Mass.; Boston University School of Medicine, 1922; served on the staff of the Lawrence Memorial Hospital, Medford; aged 50; died in East Sandwich, July 16, of coronary thrombosis.

**Edgar Parsons Cook,** Johnstown, Ohio; Cleveland Medical College, 1897; served in the medical corps of the U. S. Army during World War I; aged 76; died in the Newark Hospital, July 6.

**James H. Cook,** McMinnville, Ore.; University of Oregon Medical School, Portland, 1895; formerly a trustee of the Linfield College; aged 79; died, July 3, of heart disease.

**Pleasant A. Creswell,** Columbia, Tenn. (licensed in Tennessee in 1912); veteran of the Spanish-American War; aged 69; died recently of bronchial asthma.

**Dorwin LeRoy Culver,** St. Augustine, Fla.; University of the City of New York Medical Department, New York, 1895; aged 81; died, July 29, of hypostatic pneumonia.

**Louis Frederick Curran** ✠ Boston; Tufts College Medical School, Boston, 1917; professor of clinical medicine at his alma mater; member of the National Gastroenterological Association; on the staff of the Boston City Hospital; physician in chief at the Carney Hospital; trustee of St. Michael's College, Winooski, Vt.; aged 57; died, July 28, of coronary thrombosis.

**Gustavus Cornelius Darlington,** Reno, Nev.; Long Island College Hospital, Brooklyn, 1901; member of the Medical Society of the State of New York; served overseas during World War I; aged 80; died, July 28, of pneumonia.

**Ernest Joseph David,** Lowell, Mass.; Laval University Faculty of Medicine, Quebec, Canada, 1915; member of the Massachusetts Medical Society; district welfare physician for the city; aged 58; on the courtesy staff of St. Joseph's Hospital, where he died, July 11, of acute coronary occlusion.

**Charles Wesley Davis,** New Castle, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1895; aged 76; died, July 27, of congestive heart disease.

**Homer Augustus Davis,** Missoula, Mont.; Dartmouth Medical School, Hanover, N. H., 1892; aged 85; died, June 27.

**Jesse J. Dean,** Waco, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1897; active in the establishment of the Dean Highland school; aged 69; died, July 22, of heart disease.

**Peter De Gaetano,** Brooklyn; Long Island College Hospital, Brooklyn, 1914; aged 52; died, July 31.

**Allen Ross Diefendorf,** New Haven, Conn.; Yale University School of Medicine, New Haven, 1896; member of the Connecticut State Medical Society, American Neurological Association and the American Psychiatric Association; served as president of the Connecticut Society of Psychiatry; for many years lecturer on psychiatry at his alma mater; aged 71; died at the New Haven Hospital, July 30, of heart disease.

**Henry E. Donges,** Uvalde, Texas (licensed in Texas under the Act of 1907); aged 81; died in the Merritt Hospital, July 24.

**Francis Bernard Donohue,** Bloomingburg, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1901; at one time physician at St. Bonaventure College at Allegany; aged 69; died, July 26.

**Alexander McGill Duff Sr.,** Republic, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; for many years a director of the First National Bank of the Republic; chairman of the medical committee of civilian defense; president-elect of the Republic Rotary Club; aged 66; died in the Uniontown Hospital, July 24, of chronic nephritis.

**Lawrence Francis Dugan,** Faribault, Minn.; Marquette University School of Medicine, Milwaukee, 1924; member of the Minnesota State Medical Association; aged 45; served on the staff of St. Lucas Evangelical Deaconess Hospital, where he died, July 17, of coronary thrombosis.

**William Esser,** Manning, Iowa; Rush Medical College, Chicago, 1891; aged 86; died in Carroll, June 6, of uremia.

**William Harrison Finney** ✠ Clintonville, Wis.; Northwestern University Medical School, Chicago, 1899; served as a captain in the medical corps of the U. S. Army during World War I; for many years physician and surgeon for the Chicago and Northwestern Railroad; donated the building site for Clintonville's public library, which was named for him; aged 68; died in St. Elizabeth Hospital, Appleton, July 25, of gangrenous appendicitis.

**Chester Arthur Fleger** ✠ Ansted, W. Va.; Maryland Medical College, Baltimore, 1905; aged 62; died, July 22, of angina pectoris.

**Edward Samuel Folk** ✠ Canton, Ohio; Ohio Medical University, Columbus, 1902; since January 1939 mayor of Canton; formerly president of the city council, member of the board of education and board of health; served during World War I; aged 66; honorary member and in 1937 president of the staff of the Aultman Hospital, where he died, July 31, of coronary heart disease.

**Isar Goldofsky Fox,** Harlingen, Texas; University of Texas School of Medicine, Galveston, 1924; specialist certified by the American Board of Radiology, Inc.; president of the

Cameron-Willacy Counties Medical Society; member of the State Medical Association of Texas and the Radiological Society of North America, Inc.; roentgenologist to the Valley Baptist Hospital; aged 42; died, July 15, of acute leukemia.

**Morris Frank** ✠ Boston; Harvard Medical School, Boston, 1911; councilor of the Norfolk District of the Massachusetts Medical Society; school physician; on the staff of the Jewish Memorial Hospital; on the associate staffs of the Beth Israel and Washingtonian hospitals; physician for the Selective Service Board during World War I and recently; aged 57; died, June 17, of coronary sclerosis.

**Rawley H. Fuller,** South Boston, Va.; University College of Medicine, Richmond, 1905; member of the Medical Society of Virginia; surgeon for the Southern Railroad; aged 64; medical superintendent and owner of the South Boston Hospital, where he died, July 24, of cerebral thrombosis.

**Charlton Edwin Gamble,** Turbeville, S. C.; Medical College of the State of South Carolina, Charleston, 1907; aged 62; on the courtesy staff of the Tuomey Hospital, Sumter, where he died, July 10, of hypertension, nephritis and cerebral hemorrhage.

**Frank R. Geiger,** Columbia, S. C.; Tennessee Medical College, Knoxville, 1893; member of the South Carolina Medical Association; on the staff of the Columbia Hospital; aged 79; died, July 18, of cerebral hemorrhage.

**William Henry George** ✠ Albany, N. Y.; Albany Medical College, 1894; served on the draft board during World War I; aged 71; died, July 16, of coronary disease.

**Maurice Gerstein,** Brookline, Mass.; New York University Medical College, New York, 1896; member of the Massachusetts Medical Society; past president of the Norfolk District Medical Society; served as chief surgeon at the Jewish Memorial Hospital and on the courtesy staff at Beth Israel Hospital, Boston, where he died, July 13, of myocardial infarction, aged 73.

**William Winder Goldsborough,** Greensboro, Md.; University of Maryland School of Medicine, Baltimore, 1901; formerly state senator; served as president of the Caroline County Bank; aged 68; died in Princeton, N. J., July 13, of carcinoma of the left hand, carcinoma of the left side of the chest and chronic myocarditis.

**Burton Thomas Gordon** ✠ Pompano, Fla.; Rush Medical College, Chicago, 1910; at one time on the staff of St. Anne's Hospital, Chicago; aged 58; died in Deerfield Beach, July 2, of chronic rheumatic heart disease.

**Gus R. Griggs,** Baird, Texas (licensed in Oklahoma in 1908); aged 66; died in June of carcinoma of the lungs.

**Charles Raymond Haley,** San Augustine, Texas; Chicago College of Medicine and Surgery, 1916; first lieutenant in the medical corps of the U. S. Army during World War I; served as health officer of San Augustine County; aged 54; died recently of carcinoma of the colon.

**Henry Brown Hart,** Sarasota, Fla.; Medical School of Maine, Portland, 1899; member of the Massachusetts Medical Society; served on the board of the Cape Cod Hospital Hyannis, Mass.; formerly treasurer of the Barnstable District (Mass.) Medical Society; aged 72; died in Bradenton, July 13, of cerebral hemorrhage due to arteriosclerosis.

**Dorsey Alford Harwood** ✠ Santa Ana, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; president of the Orange County Medical Society; aged 63; on the staff of St. Joseph Hospital, Orange, where he died, July 17, of coronary insufficiency.

**Della Hertzsch,** Louisville, Ky.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1891; member of the Kentucky State Medical Association; for many years served as examining physician for the city schools; aged 82; died in the Norton Memorial Infirmary, July 12, of a fracture of the left hip from a fall and bronchopneumonia.

**John Henry Heuser,** Louisville, Ky.; University of Louisville Medical Department, 1891; member of the Kentucky State Medical Association; served during World War I; formerly on the staff of SS Mary and Elizabeth Hospital; for many years medical examiner for the Metropolitan Life Insurance Company; aged 78; died, July 1, of myocarditis.

**George Price Hill,** Summit Hill, Pa.; Medico-Chirurgical College of Philadelphia, 1904; aged 64; died, July 9, of pleurisy and chronic myocarditis.

**Marie Kirby Hopkins Humphrey,** East Rochester, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; aged 67; died in the Strong Memorial Hospital, Rochester, July 18, of pulmonary embolus due to rheumatic and arteriosclerotic heart disease.

**Henry Creath Kelker,** Cleveland; Western Reserve University Medical Department, Cleveland, 1903; for twenty-eight years physician for the Cleveland Christian Home; formerly on the staff of the Fairview Park Hospital; served as examiner for the Big Four Railroad; aged 68; died, July 11, of coronary occlusion.

**Frank Kenworthy** ✠ Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1901; a captain in the medical corps of the U. S. Army during World War I; for many years surgeon for the city department of public safety; served on the staffs of the Western Pennsylvania and Shadyside hospitals; aged 65; died, July 14, of coronary thrombosis.

**Jacob H. Kerth,** San Diego, Calif.; Medical College of Evansville, Ind., 1881; aged 87; died, July 8, of heart disease.

**John Ketterle,** St. Albans, N. Y.; Bellevue Hospital Medical College, New York, 1897; member of the Medical Society of the State of New York; a captain in the medical corps of the U. S. Army during World War I; aged 70; died, July 9, in the Mary Immaculate Hospital, Jamaica, of carcinoma of the sigmoid.

**Adolph Kroll Jr.,** Passaic, N. J.; University and Bellevue Hospital Medical College, New York, 1916; member of the Medical Society of New Jersey; member of the staffs of the Passaic General and St. Mary's hospitals; aged 51; died suddenly, July 7, in the Newark induction center of coronary occlusion.

**Oliver William Kulp,** Davenport, Iowa; State University of Iowa College of Medicine, Iowa City, 1896; formerly a captain of Company B, 54th Infantry of the Iowa National Guard; veteran of the Spanish-American War; served on the staff of the Mercy Hospital; aged 68; died, July 5, in Iowa City of coronary embolism and carcinoma of the mouth.

**Joseph Philorum Lapointe,** Harvey, N. D.; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, Que., Canada, 1917; served on the staff of the St. Aloisius Hospital; aged 52; drowned, June 25.

**Samuel Elijah Newman** ✠ St. Louis; Miami Medical College, Cincinnati, 1902; member and formerly vice president of the American Proctologic Society; on the staff of the Jewish Hospital and City Sanitarium; aged 65; died, July 17, of angina pectoris.

**James Joseph Panton,** Portland, Ore.; Long Island College Hospital, Brooklyn, 1894; member of the Oregon State Medical Society; formerly medical director of the Oregon State Penitentiary Hospital, Salem; served with the Oregon National Guard, Company G, first regiment; aged 81; died, June 19, of carcinoma of the esophagus.

**Brantly Fuller Parker,** York, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1903; member of the Medical Society of the State of Pennsylvania; served during World War I; aged 65; died, June 28, of gastric carcinoma.

**Roy C. Pope,** Niantic, Ill.; Michigan College of Medicine and Surgery, Detroit, 1901; member of the Illinois State Medical Society; aged 67; died in Boulder Junction, Wis., July 8, of valvular disease of the heart.

**Harvey Francis Rawlings** ✠ Champaign, Ill.; University of Louisville (Ky.) Medical Department, 1910; served during World War I; on the staffs of the Mercy Hospital, Urbana, and the Burnham City Hospital; aged 59; died in Jacksonville, July 14, of bronchopneumonia.

**John Luther Reeves,** Philadelphia; Howard University College of Medicine, Washington, D. C., 1923; member of the Medical Society of the State of Pennsylvania and the American College of Chest Physicians; on the staff of the Mercy Hospital; aged 43; died, July 11, of carcinoma.

**Brette Redpath Riley** ✠ Benedict, Kan.; Central Medical College of St. Joseph, Mo., 1896; served as mayor of Benedict and for many years as a member of the board of education; served during World War I; aged 72; died, July 16, of coronary embolus.

**John Wylie Robertson,** Coulterville, Ill.; Beaumont Hospital Medical College, St. Louis, 1889; member of the Illinois State Medical Society; for many years local physician and surgeon for the Illinois Central Railroad Company; aged 81; was killed, July 26, when the automobile in which he was driving was struck by a train.

**Willard B. Robinson,** Richmond, Va.; Kentucky School of Medicine, Louisville, 1886; aged 81; died, July 4.

**Armand Otto Rogers,** Ennis, Texas; Meharry Medical College, Nashville, Tenn., 1925; aged 45; died, June 21, of hypertension and myocarditis.

**Lurten Roscoe Sayler,** Dayton, Ohio; Medical College of Ohio, Cincinnati, 1888; for many years served as deputy recorder of Montgomery County; aged 81; died, July 21, of heart disease.

**Joseph Peter Schlaikowski,** Wauwatosa, Wis.; Marquette University School of Medicine, Milwaukee, 1913; served during World War I; resident physician at the Muirdale Sanatorium; aged 55; died, June 14, of coronary thrombosis.

**Henry Alvin Shaffer** ✠ Charleston, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1903; past president of the Coles-Cumberland Counties Medical Society; served during World War I; formerly health officer; president of the staff of the M. A. Montgomery Memorial Sanitarium; aged 69; died, July 15, of acute pyelitis.

**John Cresswell Slawson,** Orlando, Fla.; New York University Medical College, New York, 1898; for many years health officer of the town of Carmel, N. Y., and attending physician of the Lincolndale branch of the New York Catholic Protectory; formerly on the staffs of the Saratoga Springs Sanitarium, the Dr. Strong's, Inc., Saratoga Springs, N. Y., and the Faxton Hospital, Utica, N. Y.; aged 66; died, July 13, of chronic myocarditis.

**Gilbert Cumin Smith,** Louisville, Ky.; University of Louisville Medical Department, 1892; demonstrator of analytic chemistry at his alma mater, 1907-1908, and assistant to the chair of chemistry and toxicology, 1908-1909; also a pharmacist; aged 74; died in St. Joseph Infirmary, June 27, of carcinoma of the esophagus.

**Charles James Smyser,** New Wilmington, Pa.; Harvard Medical School, Boston, 1897; past president of the Lawrence County Medical Society; member of the Medical Society of the State of Pennsylvania; served during the Spanish-American War and World War I; on the staff of the Jameson Memorial Hospital, New Castle; aged 78; died, July 22, of arteriosclerosis.

**John Harvey Sparks,** Detroit; Meharry Medical College, Nashville, Tenn., 1914; member of the Michigan State Medical Society; aged 54; on the staffs of the Wayne Diagnostic Hospital and the Parkside Hospital, where he died, July 11.

**Thomas Frank Staley,** Bristol, Tenn.; Medical College of Virginia, Richmond, 1900; chairman of the Missionary Emergency Fund, Inc.; aged 67; died in the Henry Ford Hospital, Detroit, July 13, of acute yellow atrophy.

**Eugene Gillis Steele** ✠ Buffalo, Wyo.; Albany (N. Y.) Medical College, 1906; member of the Missouri State Medical Association; at one time on the staff of the Santa Fe Coast Lines Hospital, Los Angeles; aged 62; died, July 20, of coronary sclerosis.

**Robert Marcus Stith** ✠ Seattle; University of Pennsylvania Department of Medicine, Philadelphia, 1899; member of the American College of Chest Physicians; served as a captain in the medical corps with the 69th artillery during World War I; was chief of the division of tuberculosis control of the city health department; served as consultant for the United States Marine Hospital; medical director of the Firland Sanatorium and Isolation Hospital, Richmond Highlands, Wash.; aged 68; died, June 22, of cerebral hemorrhage.

**Cephas Swanson,** Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1907; member of the Minnesota State Medical Association; medical examiner for the Selective Service Board number 19; aged 67; on the staff of the Lutheran Deaconess Home and Hospital, where he died, July 20, of cerebral hemorrhage.

**Albert B. Sweet,** Hopkins, Minn. (licensed in Minnesota in 1880); also a pharmacist; Civil War veteran; aged 93; died in the Veterans Administration Facility, Minneapolis, July 6, of cerebral thrombosis.

**Richard Jerome Tanner,** Norfolk, Neb.; Lincoln Medical College of Cotner University, 1909; at one time known as "Diamond Dick"; aged 74; died in a Norfolk hospital, July 2, of an injury received in a fall.

**Frank Eugene Towers,** Minneapolis; University of the City of New York Medical Department, 1875; past president of the Hennepin County Medical Society; formerly served as county coroner; aged 92; died in the Parkview Sanatorium, June 1, of generalized arteriosclerosis and bronchopneumonia.

**Haworth Robert Traver,** Buffalo; University of Buffalo School of Medicine, 1917; served during World War I; aged 50; died in the Veterans Administration Facility, Canandaigua, N. Y., July 6, of coronary heart disease.

**Harrison Allen Tucker,** Brooklyn; Long Island College Hospital, Brooklyn, 1888; aged 78; died, June 28, of heart disease.

**Arthur Robert Turner** ✠ Norwalk, Conn.; Université de Paris Faculté de médecine, France, 1894; on the consulting staff of the Norwalk Hospital; aged 80; died, July 2, of coronary thrombosis.

**James Walsh** ✠ Cortland, N. Y.; New York Homeopathic Medical College and Hospital, New York, 1903; formerly school physician; chief of staff, Cortland County Hospital; aged 73; died, July 31, of coronary thrombosis.

**Stephen W. Williamson,** Dovesville, S. C.; College of Physicians and Surgeons, Baltimore, 1904; aged 72; died in the McLeod Infirmary, Florence, July 14, of myocarditis and cerebral thrombosis.

**John Wotherspoon,** Seattle; University of Glasgow Medical Faculty, Scotland, 1889; member of the Washington State Medical Association; aged 79; died, July 5, of chronic myocarditis.

**Alonzo D. Wright,** Coxs Creek, Ky.; Kentucky School of Medicine, Louisville, 1886; aged 85; was found dead in bed, July 1.

**Justus Gaige Wright,** Brooklyn; Long Island College Hospital, Brooklyn, 1899; member of the Medical Society of the State of New York; on the staff of the Carson C. Peck Memorial Hospital; consulting pediatrician to the Cumberland, Prospect Heights and the Brooklyn Nursery and Infants' hospitals; aged 65; died at his summer home in Mattituck, N. Y., July 27.

**Goldman McDonald Young** ✠ Postell, N. C.; Lincoln Memorial University Medical Department, Knoxville, Tenn., 1916; aged 58; died, July 9, of carcinoma of the stomach.

## DIED WHILE IN MILITARY SERVICE

**William Ambrose Hutchinson,** Texarkana, Ark.; Tulane University of Louisiana School of Medicine, New Orleans, 1924; served as secretary of the Bowie County (Texas) Medical Society in 1934 and as president in 1938; in 1931 was commissioned a first lieutenant in the medical corps of the Texas National Guard, in July 1932 promoted to captain and in March 1940 became a major; began active duty in the medical corps of the U. S. Army (National Guard) in November 1940; was promoted to the grade of lieutenant colonel in June 1942; had been in command of a hospital at Eritrea, Africa; was killed in an airplane crash in the Middle Eastern area of North Africa, February 23.

**William Harris Funk** ✠ Captain, M. C., U. S. Navy, Washington, D. C.; Johns Hopkins University School of Medicine, Baltimore, 1920; U. S. Naval Medical School, 1921; entered the medical corps of the U. S. Navy in June 1920; served on many assignments in various ports of the world where the Navy maintains its stations; specialist certified by the American Board of Internal Medicine; diplomate of the National Board of Medical Examiners; fellow of the American College of Physicians; aged 50; died, January 6, in Kodiak, Alaska.

**Adam George Heilman** ✠ Lieutenant Colonel, M. C., U. S. Army, Washington, D. C.; University of Pennsylvania School of Medicine, Philadelphia, 1913; U. S. Army Medical School, 1922; served during World War I; entered the medical corps of the U. S. Army as a first lieutenant in 1920; aged 57; died in the Walter Reed General Hospital, August 12, of bacterial (Streptococcus fecalis) endocarditis.

**Pascasio Quinones-Chacon** ✠ Baltimore; George Washington University School of Medicine, Washington, D. C., 1936; member of the Medical Association of Puerto Rico; began active duty as first lieutenant in the medical reserve corps of the U. S. Army in February 1942; aged 32; was killed in an airplane accident in Puerto Rico, Oct. 1, 1942.

**Robert Corkill Quine,** San Diego, Calif.; Rush Medical College, Chicago, 1935; commissioned a captain and later a major in the medical reserve corps of the U. S. Army; a flight surgeon; aged 41; was killed in an airplane crash at Gunnison, Colo., July 19.

# Bureau of Investigation

## DANGEROUS TO HEALTH
### When Used as Directed

[EDITORIAL NOTE.—These abstracts differ from other abstracts of Notices of Judgment issued by the Food and Drug Administration of the Federal Security Agency which have appeared in these pages in that they include reference to the fact that these nostrums were specifically declared to be dangerous when used in accordance with the directions given on the label by the manufacturer. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the date of shipment; (4) the composition; (5) the type of nostrum; (6) the reason for the charge of misbranding, and (7) the date of issuance of the Notice of Judgment—which is considerably later than the date of the seizure of the product and somewhat later than the conclusion of the case by the Food and Drug Administration.]

**Alcoban.**—Maffett Sales Corporation, Seattle. Shipped between Feb. 19 and Sept. 23, 1941. Composition: capsules containing emetine hydrochloride in amounts varying from 0.05 to 0.18 grain, with ephedrine hydrochloride, pilocarpine hydrochloride and milk sugar. Misbranded because dangerous to health when used in the dosage and with the frequency and duration suggested on label and because claim on carton, "An aid in curbing the liquor habit," and similar statements in accompanying circular were false and misleading since this product would not be an appropriate or effective treatment for that purpose.—[*D. D. N. J., F. D. C. 606; February 1943.*]

**Breatheasy Kits and Inhalant.**—Breatheasy Distributors, Inc., Seattle. Shipped between Nov. 27, 1940 and April 26, 1941. Composition: government chemists reported finding that the product had the activity of 3 per cent synthetic racemic epinephrine hydrochloride. Misbranded because dangerous to health when used in the dosage or with the frequency or duration prescribed on bottle label and in accompanying booklet. Also misbranded because statements in booklet gave the impression that the product was a safe, appropriate and efficacious treatment for asthma, hay fever, dermatitis, eczema, chronic bronchitis and head colds. Further misbranded because carton label failed to bear common or usual names of active ingredients, a statement of the quantity of contents and the name and place of business of manufacturer, packer or distributor.—[*D. D. N. J., F. D. C. 546; November 1942.*]

**Bromo-Caps.**—Parke, Davis and Company, Detroit. Shipped April 11, 1941. Composition: in each capsule essentially 2.3 grains of acetanilid, 4.4 grains of aspirin and ¾ grain of caffeine. Adulterated because strength differed from that claimed on label, namely, that each capsule contained 3½ grains of acetanilid. Misbranded because dangerous to health if used in dosage or with frequency or duration suggested on label. Also misbranded because of misleading name, since no bromine or compound thereof was present. Further misbranded because of false and misleading claims that product contained no narcotic drugs and was a quick, sure, scientific remedy which would take the place of aspirin and habit forming headache powders and liquids, since the latter claim created the impression that the product contained neither dangerous drugs nor aspirin. Misbranded again because of misrepresentations that the preparation would give relief and constitute an adequate treatment for rheumatic pains, colds, toothache, mental fatigue, menstrual pains, feverish conditions, sea or car sickness or overindulgence in food or drink. Misbranded also because label did not list the common or usual names of the active ingredients, other than acetanilid, and the quantity or proportion of the latter was not correctly declared. Further charges of misbranding were: Labels failed to bear adequate directions for use or warnings that, because of acetanilid content, frequent or continued use might be dangerous, causing serious blood disturbances, anemia, collapse or dependence on that drug; also, label did not caution against giving the product to children or using it in those pathologic conditions wherein it might be dangerous to health, or warn against unsafe dosage or methods or duration of administration.—[*D. D. N. J., F. D. C. 601; February 1943.*]

**Cold Tablets and Capsules.**—Upjohn Company, Kalamazoo, Mich., and New York. Shipped between Sept. 25, 1940 and Feb. 14, 1941. Composition: included acetanilid, a quinine salt, camphor, podophyllin and aloin. Products were variously labeled "Capsules Cold Special," "Upjohn Cold Special," "Cold Special No. 2" and "Swiss Capsules." All misbranded because dangerous to health when used in dosage and with frequency and duration suggested in labeling. Further misbranded because labeling did not, in most instances, bear adequate directions for use, since such directions as were given would have caused the products to be dangerous to health. Further misbranded because labeling failed to warn sufficiently against use by children and in those pathologic conditions wherein the tablets and capsules might be dangerous to health. Also misbranded because labels failed to caution against use in cases of nausea, vomiting, abdominal pain or other symptoms of appendicitis or continued use which might cause serious blood disturbances, anemia, collapse or a dependence on the drug. Misbranded finally because of false and misleading representation that the tablets and capsules were a remedy for simple colds.—[*D. D. N. J., F. D. C. 602; February 1943.*]

**Lounbach' Paste.**—Merz and Company Chemical Works, Inc., Newark and East Orange, N. J. Shipped Aug. 16, 1940. Composition: soap, water and about 2 per cent each of alcohol and potassium iodide. Misbranded because dangerous to health when used, as an abortifacient in the dosage or with the frequency or duration recommended in labeling.—[*D. D. N. J., F. D. C. 607; February 1943.*] (Another consignment, shipped Jan. 25, 1942, by the Doctors Pharmacy, Milwaukee, was declared misbranded under *D. D. N. J., F. D. C. 608* for the reason given above.)

**Mrs. Moffat's Shoo Fly Powders for Drunkenness.**—M. F. Groves' Son and Company, Philadelphia. Shipped Nov. 2, 1940. Composition: tartar emetic. Misbranded because dangerous to health when used in the dosage or with the frequency or duration suggested in labeling and also because statement "for drunkenness" was false and misleading.—[*D. D. N. J., F. D. C. 605; February 1943.*]

**Nature's Minerals Compound.**—Nature's Mineral Company, Indianapolis, also known as Nature's Minerals Company and Nature's Mineral Food Company. Shipped between Aug. 26, 1940, and Jan. 24, 1941. Composition: (preparation in powder and tablet form), essentially compounds of calcium, magnesium, iron and sodium, phosphates, carbonates, sulfates, chlorides, sulfur and fluorine. Misbranded because dangerous to health when used in the dosage or with the frequency or duration suggested in the labeling, since it contained a poisonous substance, fluorine. Further misbranded because of false and misleading representations on cartons and bottles that the preparation would supply minerals deficient in the ordinary diet. [*D. D. N. J., F. D. C. 541, 542 and 545; November 1942.*] Consignments of a product called simply "Nature's Minerals" and shipped by the aforenamed concern, between Sept. 13, 1940 and April 18, 1941 and reported identical in composition, were subjects of *D. D. N. J., F. D. C. 543 and 544, November 1942.* One charge of misbranding was under the representations that the product would be efficacious in treating or preventing cancer, arteriosclerosis, diabetes, stomach, blood, kidney and bladder disorders, gallstones and some other things. Cases Nos. 544 and 545 also included the name of P. G. Jurich, Pasadena, Calif., as a shipper.

**Special Formula Tablets and McNeal's Laxative Cold Tablets.**—Arner Company, Inc., Buffalo, N. Y. Shipped Dec. 16, 1940. Composition: (the products were identical) in each tablet acetanilid (approximately 1 grain), quinine sulfate (approximately 0.38 grain), a laxative plant drug and a small amount of atropine. McNeal product misbranded because dangerous to health when used in the dosage or with the frequency or duration suggested in the labeling. Also misbranded because labeling failed to give adequate directions for taking it and did not sufficiently caution against use by children or in those pathologic conditions in which it might be dangerous to health, or warn against unsafe dosage or methods or duration of administration or application, for protection of users. "Special Formula Tablets" misbranded because labels did not bear common or usual names of the active ingredients or declare the amounts or proportions of acetanilid and atropine present.—[*D. D. N. J., F. D. C. 547; November 1942.*]

**Tabknoll Three Bromides Effervescent.**—H. G. Knoll and Company, Inc., New York. Shipped Jan. 6, 1941. Composition: ammonium, potassium and sodium bromides. Misbranded because dangerous to health when taken in the dosage or with the frequency and duration prescribed in the labeling, because latter failed to give adequate directions for use and to bear sufficient warnings against use when it might be dangerous to health, or caution against unsafe dosage or duration of administration, in such manner and form as are necessary for protection of users.—[*D. D. N. J., F. D. C. 548; November 1942.*]

**Whitehall's (Dr.) Compound Tablets.**—Dr. Whitehall Megrimine Company, South Bend, Ind. Shipped between Nov. 27 and Dec. 3, 1940. Composition: acetanilid, sodium salicylate and plant material. Misbranded because dangerous to health if taken in the dosage or with the frequency or duration prescribed in the labeling, since such use might cause serious blood disturbances, anemia, collapse and a dependence on the drug. Further misbranded because labeling failed to give adequate directions for use, since it did not provide for a limit as to the duration or frequency of administration. Misbranded also because labels failed to carry adequate warnings against use by children or in conditions in which the product might be dangerous to health, or to caution against unsafe dosage or methods or duration of administration. Misbranded, finally, because label gave the false impression that the product was an appropriate treatment for the conditions described, whereas it was not, but actually a dangerous drug.—[*D. D. N. J., F. D. C. 549; November 1942.*]

**Zerbst's Capsules.**—Zerbst Pharmacal Company, St. Joseph, Mo. Shipped Jan. 20, 1941. Composition: capsules (in 25 cent package) each containing acetanilid (1¼ grains per capsule) with caffeine, resinous material, camphor, capsicum, aloin and asafoetida; (50 cent package) acetanilid (2½ grains per capsule) and a laxative plant drug, not named. Both packages misbranded because dangerous to health when used according to directions on the label. Further misbranded because labels failed to bear adequate warnings against use by children or in those pathologic conditions in which product might be dangerous to health, or to caution against unsafe dosage or duration of administration, for protection of users, since no warning was given against use in the presence of appendicitis symptoms or with reference to possibility of serious blood disturbances following use of acetanilid, or any warning that frequent or continued use might result in dependence on the drug. The 50 cent package was found misbranded also because, among other things, it was falsely represented that these capsules would break up a cold, and label failed to give common or usual name of each active ingredient or declare quantity of contents of the package.—[*D. D. N. J., F. D. C. 550; November 1942.*]

# Correspondence

## THE EMERGENCE OF THE CHRONIC PATIENT

*To the Editor:*—Of late years the students of vital and social statistics have been calling our attention to the remarkable increase in longevity which is having such a profound influence on our way of living. As the length of our days on earth is increased we find ourselves living longer, in health and otherwise, with people who must live longer with us. Youth, being confronted with the problems of age, must share them. Youth too may be stricken by long-term disease, as in the case of rheumatic fever with its complications and sequelae. Against the satisfaction and joy of preventing and curing illness in the earlier years we now have the specter of the degenerative and malignant diseases which are more characteristic of the later years.

The "acute" hospital, which has chosen and specialized in emergencies during the earlier years of our lives, can have only one response to the needs of the chronic patient with whom philanthropist, physician, nurse and social worker must now live longer. We have learned to be patient with the lame, the halt and the blind, and we must learn to be patient with those who are sick with a long-term disease. Medical science is equipped to meet the challenge in this realm and should welcome the opportunity. The beggar must not be turned away from our doors for fear that he may break our hearts.

A reasonable proportion of long-term patients who still require intensive medical care should be retained in general hospitals, and the establishment of independent hospitals for chronic disease, at comparatively greater expense if the job is to be done right, and at a distance, should be discouraged. The qualifying adjectives "acute" and "chronic" have no place in connection with institutions built for the scientific care of the sick. For our help in reconsidering the claims of the long-term patient to the attention of the modern hospital we have a number of recent developments which owe their existence to the war and to the threat of insecurity generally.

Provisions for social security which preceded and subsequently went hand in hand with the idea of the four freedoms include more public funds for the care of patients who are chronically ill and cannot finance themselves. (Poverty and chronic disease lie within a vicious circle which must be broken somewhere.) Furthermore, we are witnessing an extension of voluntary group insurance schemes which will confer more benefits all around, over longer periods of time, for those who can afford it. Direct income from patient sources will also be noticeably increased. For these three reasons, hospitals will be less dependent on philanthropy and ultimately less dependent on voluntary medical service. Because of these new or improved sources of income the financial reason for the transfer of long-term patients from the "acute" hospital to a segregated and isolated institution independently maintained for chronic disease, at a time when they may need scientific care most, will disappear. Such patients will be retained longer in general hospitals, where they belong. The duration of their illness, which now differentiates them so artificially from short-term patients, will no longer appear as a criterion for their admission or retention.

Apart from economic developments which will favor the retention of the long-term patient, we have the following to consider: (*a*) the increased interest of the physician, social worker and public generally in chronic disease, (*b*) the provision of full time opportunities in hospitals and the remuneration of physicians for medical service in hospitals and dispensaries generally, (*c*) the increase of laboratory facilities in hospitals where qualified physicians who have selective interests in the various categories of chronic disease can develop their special talents along these lines and (*d*) the utter inadequacy and indecency of existing facilities for the care of long-term patients. Thus the second major reason for transfer will disappear, namely the lack of interest in patients with a long drawn out illness. The presence of these patients in hospitals where they are under control over longer periods of time, either continuously or in divided visits, gives to the scientific physician greater opportunities to study the remote results of treatment than ever before and, if he is freed from financial worry while having the additional opportunities of the laboratory, he will welcome the change. In passing, I might add that the lack of interest of the doctor in chronic disease encourages quackery as a possible relief to the uneducated patient.

These new trends indicate that chronic disease is rapidly emerging as an acute social and medical problem, and it will not be denied if for no other reason because it is beginning to strike home to many of us who are responsible for hospital progress. Moreover, the war will leave us with a demand for the rehabilitation of the wounded in our armed forces, many of whom will be in the long-term classification. This will doubtless increase our respect for the patient suffering from chronic disease and stimulate adequate provisions for his hospitalization.

The medical profession is greatly concerned with the trends of social security in its broadest implications and now has the opportunity of cooperating in the solution of this vexing problem, while benefiting itself in many desirable ways. It is now up to the hospitals and their medical boards to formulate a program without delay. In competition with government, they have always done better in such matters thus far.

E. M. BLUESTONE, M.D., New York.
Director, Montefiore Hospital.

## "INSECT VECTORS OF POLIOMYELITIS"

*To the Editor:*—In reading your editorial on "Insect Vectors of Poliomyelitis" in the August 28 issue of THE JOURNAL I was struck by this statement: "The dominant species in each group were green bottleflies and blowflies, the common housefly being present in small numbers in only two of the four positive specimens."

The common housefly is such an important vector of dysentery that it seemed strange that it had not been more seriously considered in these investigations concerning poliomyelitis. I wondered at once what type of bait had been used in catching the flies used in the experiments by Trask, Paul and Melnick. I had missed their articles in the *Journal of Experimental Medicine,* but on looking up their publication I see that the bait used principally was fish. This bait is somewhat attractive to the housefly, but, of course, much more so to bottleflies and blowflies. Had a fermenting bait been used it is far more than probable that the dominant species of flies caught would have been houseflies, and the results might have been totally different.

Control of the housefly is a major problem in Army sanitation and it is especially important that the role of this insect with respect to the spread of poliomyelitis be made clear. If any experimental work is being done during your current epidemic in Chicago, it is suggested that efforts be made to trap houseflies and repeat the experiments of Trask, Paul and Melnick.

CHARLES G. SOUDER,
Colonel, M. C., U. S. Army.

# Miscellany

## THE AMERICAN MEDICAL ASSOCIATION AND THE CULTIVATION OF THE CINCHONA TREE IN THE UNITED STATES

ERWIN H. ACKERKNECHT, M.D.
BALTIMORE

It is now common knowledge that the Japanese in taking Java cut off the source of almost the entire prewar quinine supply of the world. It is equally well known that the resulting quinine shortage is still, in spite of many ingenious and valuable countermeasures, one of the most serious problems of medical warfare. The American Medical Association can rightly be proud of having been, seventy-five years ago, the protagonist of a plan which, if it had been executed, would have saved us our present difficulties.

In 1738, a hundred years after the introduction of the Peruvian bark into our pharmacopeia, La Condamine had already foreseen the exhaustion of the South American supply as a consequence of the purely destructive methods of "production" in New Granada, Ecuador, Peru and Bolivia. After a hundred years had passed the situation had grown so dangerous indeed that the Dutch and the English started cultivating the cinchona tree in their own colonies, the former in 1854 in Java, the latter in 1860 in the Neilgherry Hills of southern India.

The Transactions of the fifteenth annual session of the American Medical Association, held in 1864 in the city of New York, contain a little memorandum of Dr. D. J. Macgowan (apparently an army surgeon) of Washington, D. C., on the "Naturalization of Cinchona on the Eastern Continent."[1] Macgowan dealt with the Dutch and English experiments and recommended that they also be tried in Haiti. The assembly reacted favorably to the suggestion, and on the motion of Dr. J. H. Griscom, the famous New York Quaker and sanitarian, appointed a committee composed of three of its most distinguished members, Joseph M. Smith, E. R. Squibb and J. H. Griscom, to confer with the Haitian minister[2] on the subject.

Three years later, in 1867, the Medical Society of Wayne County, Mich., submitted to the eighteenth annual session of the American Medical Association a paper of its member Dr. J. M. Bigelow which examined the whole cinchona situation in more detail and boldly and rightly asked the introduction and cultivation of the cinchona trees in the United States.[3] Dr. Bigelow designated western Texas, Arizona or Lower California as best fitted for such plantations. On the motion of Dr. W. B. Atkinson (Pennsylvania) a committee consisting of J. M. Toner (District of Columbia), F. Howard (District of Columbia) and C. A. Lee (New York State), was appointed to "memorialize" Congress on this vital question.[4] In the next year, 1868, Dr. Toner read a report of the committee in the Section on Chemistry and Materia Medica, and a new committee, composed of Dr. L. J. Deal (Pennsylvania), T. A. Logan (California) and J. M. Bigelow (Michigan), was elected to memorialize Congress.[5] For seven years this committee, under the leadership of Dr. Deal, was to carry on a vigorous, intelligent fight for the cultivation of the cinchona tree in the United States.

At the twenty-first annual session, in 1870, Dr. L. J. Deal submitted a report of the committee, consisting mainly of a proposed memorial to Congress.[6] This memorial was the most important and substantial document published during this action of the American Medical Association. It starts with an explanation of the medical value of quinine and then gives some interesting data on the economic implications of the problem: For example, from 1859 to 1865, $2,287,250 worth of bark and quinine salts were imported into the United States; between 1861 and 1865 the United States Army purchased 1,198,000 ounces of quinine (the average annual consumption of the United States before World War II was 5,000,000 ounces). The memorial describes the danger arising from the exhaustion of the Peruvian supply and recommends the cultivation of cinchona in California, which seemed to be even better suited for such an enterprise than India. The aid of the California State Board of Agriculture and the Sacramento Medical Society had already been secured. The memorial concludes:

> The American Medical Association therefore asks, in view of the foregoing facts, that the Congress of the United States would appoint a commission of scientific men for the following purpose:
>
> 1. To determine what portion, if any, of the public domain of the United States will produce the cinchona, and which may be set apart for this purpose.
>
> 2. To determine what species may be best transplanted and will furnish the greatest amount of active principles.
>
> 3. That they be authorized to visit such South American countries as they may deem necessary in order to determine these points, employ a competent botanist to assist them, and that our consuls in such States be instructed to further these investigations.
>
> 4. That they be empowered to negotiate for, and obtain a proper quantity of seeds and plants.[7]

In 1872 Dr. L. J. Deal reported "a gratifying progress, Congress having been memorialized with a favorable prospect of success." A second memorial to Congress was submitted.[7a] The transactions of 1874 contain a more detailed report of the committee which still sounds rather optimistic: Since 1868 "three memorials had been presented to Congress. The last . . . by Mr. Scott of Pennsylvania in the Senate, and by Mr. Kelley of Pennsylvania in the House." The latter wrote to Dr. Deal that he could not assure him of speedy help from Congress in the matter but that continuous pushing of the matter would probably result in success. The committee had obtained the support of the Botanical Gardens in Washington, D. C., of the Department of Agriculture and of the Horticultural Society. President Grant, in his message relating to the purchase of San Domingo, had advanced the argument that the climate and the soil of this island were suitable for the cultivation of cinchona. The committee was continued.[8]

But, alas, at the twenty-sixth annual session in 1875, after a "report of progress," the committee was discontinued.[9] We do not know the exact reasons and motivations for this step but, though regrettable, it is only human that after seven years of incessant endeavor the Association grew tired of preaching to deaf ears and did not, like Jacob, go on for another seven years of bondage. In this action, which seemed only an episode but has now become so consequential, the American Medical Association showed a considerable degree of informedness and of foresight in the public interest. Like so many plans of prevention, its plan probably suffered from looking more costly than expedient. The failure seems no reason to give up in similar situations in which our scientific conscience commands unpopular proposals in the public interest. On the contrary, it seems to be rather an admonition to be still more perseverant.

1900 East Monument Street.

From the Institute of the History of Medicine, Johns Hopkins University.

1. Macgowan, D. J.: Naturalization of Cinchona on the Eastern Continent, Tr. A. M. A. **15**: 151-154, 1864.
2. Tr. A. M. A. **15**: 31, 1865.
3. Cultivation of the Cinchona Trees in the United States, Tr. A. M. A. **18**: 37-40, 1867.
4. Tr. A. M. A. **18**: 40, 1867.
5. Tr. A. M. A. **19**: 149, 1868.
6. Tr. A. M. A. **21**: 153-160, 1870.
7. Tr. A. M. A. **21**: 159-160, 1870.
7a. Tr. A. M. A. **23**: 193, 1872.
8. Tr. A. M. A. **25**: 139-140, 1874.
9. Tr. A. M. A. **26**: 44, 1875.

# Medical Examinations and Licensure

## COMING EXAMINATIONS AND MEETINGS

### BOARDS OF MEDICAL EXAMINERS
### BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Oct. 2, page 305.

### NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Nov. 15-17 and Jan. 17-19. Sec., Dr. J. S. Rodman, 225 S. 15th St., Philadelphia.

### EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Written. Part I.* Various centers, Jan. 21. Final date for filing application is Oct. 21. Sec., Dr. P. M. Wood, 745 Fifth Ave., New York 22, N. Y.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I.* Locally, Feb. 12. Final date for filing application is Nov. 15. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh 6, Pa.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Written and Oral. Part II.* Chicago, Jan. 21-22. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans, Louisiana.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, October; Los Angeles, Feb. 2-5 (provided 50 applicants are accepted). Sec., Dr. Dean M. Lierle, University Hospital, Iowa City, Iowa.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Feb. 4. *Oral.* Philadelphia, March 25-26, and San Francisco, May 6-7. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Written.* Locally, Oct. 30. *Oral.* Locally, Dec. 20-21. Final date for filing application is Sept. 30. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C

AMERICAN BOARD OF RADIOLOGY: February. Final date for filing application is Dec. 15. Sec., Dr. B. R. Kirklin, 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF UROLOGY: *Oral.* Chicago, February. *Written.* Various centers, December. Final date for filing application is Nov. 1. Sec., Dr. Gilbert J. Thomas, 1409 Willow St., Minneapolis, Minn.

# Bureau of Legal Medicine and Legislation

## MEDICOLEGAL ABSTRACTS

**Venereal Diseases: Constitutionality of City Ordinance Requiring Treatment of Infected Persons Convicted of Prostitution.**—By Little Rock city ordinances prostitution is made a criminal offense and the city health officer is required to ascertain by necessary tests and examinations whether or not a person convicted of prostitution has any venereal disease. Any evidence so acquired is not to be used in any criminal prosecution against the person convicted. If the convicted person is found to have a venereal disease in a communicable stage and if she fails to take or submit to treatment adequate for the protection of public health, the city health officer is authorized to commit her to an appropriate institution for treatment, provided only that she can be committed without endangering life. The plaintiff was convicted of prostitution and was thereafter examined by the city health officer and was found to have venereal disease in a communicable stage. She was thereafter ordered quarantined in a health center maintained by the United States government in Hot Springs, Ark. She then filed a petition for a writ of habeas corpus, contending that her detention was illegal because the ordinances purporting to authorize it were unconstitutional and void. The trial court granted the writ and the defendants, the city of Little Rock, the city health officer and the county sheriff, appealed to the Supreme Court of Arkansas.

The determining question here presented, said the Supreme Court, is whether or not the ordinances of Little Rock in question are valid as being within the police power of the city. Admittedly, the city has power to declare prostitution a criminal offense. The proceeding under which the plaintiff was detained is not a criminal proceeding, however, but is one in the interest not only of the plaintiff but of the public. It is a proceeding to compel her to be quarantined and segregated from the public to the end that she may be cured of the venereal disease with which she is infected and thus not communicate it to others. When a cure is effected the authority to detain her is at an end. Courts, the court continued, in testing the validity of a regulation, must resolve all doubts in favor of the legislative action and must sustain the regulation unless it appears to be clearly outside the scope of reasonable and legitimate regulation. The police power of the state is founded in public necessity and this necessity must exist in order to justify its exercise. It is always justified when it can be said to be in the interest of the public health, public safety and public comfort, and in such instances private rights must yield to their security under reasonable laws. Can there be any doubt that the legislature might enact valid legislation similar to the ordinances here in question? We think not. If it could, then it can and has delegated this power to municipalities. Section 9543, Pope's Digest, authorizes municipalities to make ordinances to provide for the safety, preserve the health, promote the prosperity and improve the morals, order, comfort and convenience of the inhabitants thereof. Section 9589 further gives municipalities power to prevent injury or annoyance within the limits of the corporation, from anything dangerous, offensive or unhealthy. These two sections constitute a delegation to municipalities of the state's power to legislate in protection of public health. Exercise of the delegated powers by the city in the ordinances here presented must be held to be within the grant, unless it can be said that the power conferred on the city health officer is unreasonable. The court could not say that the power conferred on the health officer was "clearly outside the scope of reasonable and legitimate regulation."

Section 9679, Pope's Digest, authorizes a city council to establish a board of health, with jurisdiction for 1 mile beyond the city limits, and for quarantine purposes, in cases of epidemic, 5 miles. The trial court held that that statute denied the city health officer the right to quarantine plaintiff outside the city or county beyond the limits indicated in the statute. The statute referred to, said the Supreme Court, simply means that the jurisdiction of the health officer extends for 1 mile beyond the city limits, or for 5 miles for quarantine purposes, in cases of epidemics. It has no reference to the place a person may be confined for quarantine purposes, but only to the extent of the jurisdiction beyond the city limits for the better protection of the inhabitants of the city. Section 6438, *ibid.*, expressly requires the city health officer to perform the duties prescribed for him by the regulations of the state board of health. A regulation of the state board of health, promulgated under that authority, provided that any health authority should, when in the exercise of his discretion he believed that the public health required it, commit any person apprehended, examined and found afflicted with an infectious disease and who refused or failed to take treatment adequate for the protection of the public health to a hospital or other place in the state for such treatment if the commitment could be done without endangering the life of the patient. This regulation, the court concluded, was authority to commit the plaintiff outside of Little Rock and to confine her where she was confined in Hot Springs.

The Supreme Court accordingly reversed the judgment of the trial court and remanded the plaintiff to the custody of the sheriff for isolation and quarantine.—*City of Little Rock v. Smith, 163 S. W. (2d) 705 (Ark., 1942).*

# Society Proceedings

## COMING MEETINGS

Aero Medical Association of the United States, Cincinnati, Ohio, Oct. 26-27. Dr. David S. Brachman, 5440 Cass Ave., Detroit, Secretary.

American Academy of Ophthalmology and Otolaryngology, Chicago, Oct. 10-13. Dr. W. L. Benedict, 102 Second Ave. S.W., Rochester, Minn., Secretary.

American Public Health Association, New York, Oct. 12-14. Dr. Reginald M. Atwater, 1790 Broadway, New York, Executive Secretary.

Association of Military Surgeons of the United States, Philadelphia, Oct. 21-23. Colonel James M. Phalen, Army Medical Museum, Washington, D. C., Secretary.

Delaware, Medical Society of, Wilmington, Oct. 12-13. Dr. W. O. La Motte, 601 Delaware Ave., Wilmington, Secretary.

Inter-State Postgraduate Medical Association of North America, Chicago, Oct. 26-29. Dr. Arthur G. Sullivan, 16 North Carroll St., Madison, Wis., Managing Director.

Oklahoma City Clinical Society, Oklahoma City, Oct. 18-21. Dr. Clark H. Hall, 117 North Broadway, Oklahoma City, Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 25-29. Dr. J. D. McCarthy, 1036 Medical Arts Bldg., Omaha, Secretary.

Radiological Society of North America, Chicago, Nov. 29-Dec. 3. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.

Seaboard Medical Association, Richmond, Va., Nov. 30-Dec. 2. Dr. Clarence P. Jones, 3117 West Avenue, Newport News, Va., Secretary.

Southern Medical Association, Cincinnati, November 16-18. Mr. C. P. Loranz, Empire Building, Birmingham, Alabama, Secretary.

Virginia, Medical Society of, Roanoke, Oct. 25-27. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.

# Current Medical Literature

## AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1933 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

### American J. Digestive Diseases, Fort Wayne, Ind.

**10**:241-282 (July) 1943

Effect of Atropine on Gastrointestinal Canal and Its Glands. V. E. Henderson and M. O. Sweeten.—p. 241.
Newer Concepts in Treatment of Diabetes Mellitus with Protamine Insulin. E. Tolstoi.—p. 247.
Pruritus Ani. A. J. Cantor.—p. 254.
Effect of Dog's Bile, Certain Bile Acids and India Ink on Bilirubinemia and Excretion of Bromsulphalein. A. Cantarow and C. W. Wirts Jr.—p. 261.
Some Effects of High Fat Diets on Intestinal Elimination. 1. Helen L. Wikoff, S. D. Koonce and H. Jane McGuire.—p. 266.
Cardiospasm: Successful Treatment by Esophagogastrostomy. J. Lichstein.—p. 271.
Digestive Disturbances in Early Cardiac Failure. A. W. Oelgoetz.—p. 275.
Tannin Control of Ileostomy. M. Peelen and F. F. Yonkman.—p. 277.

### American Journal of Medical Sciences, Philadelphia

**206**:1-140 (July) 1943

Atypical Pernicious Anemia of Young Adults. S. O. Schwartz and Helen Legere.—p. 1.
Dynamics of Air Borne Infection. W. F. Wells and Mildred W. Wells.—p. 11.
*Studies on Bone Marrow in Vitro: I. Cellular Pattern and Behavior of Explanted Bone Marrow. M. Rachmilewitz and A. Rosin.—p. 17.
*Tissue Culture Studies on Cytotoxicity of Bactericidal Agents: II. Effect of Tyrothricin, Gramicidin and Tyrocidine on Culture of Mammalian Spleen. W. E. Herrell, Dorothy Heilman and R. P. Gage—p. 26.
Clinical Significance of Loud Aortic and Apical Systolic Heart Murmurs without Diastolic Murmurs. L. A. Baker, H. B. Sprague and P. D. White.—p. 31.
Magnesium Sulfate in Paroxysmal Tachycardia. L. J. Boyd and D. Scherf.—p. 43.
Criteria for Differentiating Deep $Q_3$ Electrocardiograms from Normal and Cardiac Subjects. M. Mazer and J. A. Reisinger.—p. 48.
Dissecting Aneurysm of Aorta. R. B. Logue.—p. 54.
Arteritis in Rats with Experimental Renal Hypertension. W. J. Cromartie.—p. 66.
*Management of Obesity with Emphasis on Appetite Control. N. H. Colton, H. I. Seagal, A. Steinberg, F. R. Shechter and N. Pastor.—p. 75.
Urinary Elimination of Phenolsulfonephthalein Injected into Cerebrospinal Cavity in Schizophrenia and General Paresis. S. Androp, H. E. Ratcliffe and S. Katzenelbogen.—p. 866.

**Studies on Bone Marrow in Vitro.**—Rachmilewitz and Rosin obtained bone marrow from the tibias of 6 to 8 week old rabbits. The containers used for explantation were glass tubes 1.5 cm. in height and 8 mm. in diameter. The bone marrow fragment of the size of 3 cubic millimeters was placed immediately after removal from the tibia in the medium, consisting of 3 drops of rabbit's plasma, 3 drops of Tyrode solution and 1 drop of diluted chick embryo extract. The tissue fragments were planted at the time when the plasma began to coagulate, so that they remained suspended in the upper layers of the medium. The tightly closed tubes were incubated at 37 C. After incubation the plasma clot containing the bone marrow explant was removed and fixed. Experiments were carried out with bone marrow of 26 rabbits. The bone marrow of 12 animals showed predominant leukopoiesis; of 8, predominant erythropoiesis. In the bone marrow of 6 animals myeloid and erythroid cells were present in nearly equal proportions. The material was fixed in Zenker's and Helly's fluid. After the specimens had been embedded in celloidin-paraffin, serial sections 4 microns thick were made and stained with hematoxylin-eosin. Some of the sections were stained with Giemsa stain. The object of this investigation was to establish a physiologic model which would help in the analysis of the factors which govern normal and pathologic blood cell formation in the bone marrow. The method of bone marrow explantation and the observations made give reason to assume that this may be possible. The bone marrow in vitro continues for a certain period of time the specific functional activity, even at an increased rate. This period of functional activity of bone marrow in vitro can be made use of in the study of the factors which affect the bone marrow function. Maturation and multiplication of white and red cells was observed to take place in the explanted bone marrow; maturation of polymorphonuclear leukocytes in vitro was proved by differential cell counts. The period of functional activity of the explanted bone marrow is followed by depletion of the marrow parenchyma and fibroblastic proliferation of the stroma.

**Cytotoxicity of Bactericidal Agents.**—In order to compare the relative cytotoxic effect of tyrothricin and its fractions gramicidin and tyrocidine, Herrell and his collaborators made experiments in which tissues were grown in a plasma clot in Carrell flasks for a period of four days. Rabbit spleen was used as a source of tissue because it is fairly homogeneous and provides a good source of large wandering cells or macrophages. The authors conclude that when the toxicity of the products of Bacillus brevis is determined by their ability to inhibit the migration of macrophages from the normal rabbit's spleen in a medium composed of serum, plasma and chick embryo extract, it appears that gramicidin is most toxic; tyrothricin is next in order of toxicity, and tyrocidine is much less toxic than either gramicidin or tyrothricin. The greater part of the cytotoxicity of tyrothricin is accounted for by its content of gramicidin. The authors emphasize that the cytotoxicity of products of B. brevis is low compared with that of a number of other germicides. This agrees with the absence of deleterious effects on the tissues when aqueous suspensions of these substances are used in the local treatment of infections.

**Obesity and Appetite Control.**—According to Colton and his associates the restriction of food intake is still the basic principle in all successful attempts at treatment. Dietary restriction over a long period of time is exceedingly difficult in most cases without the aid of some agent that depresses the appetite. The authors treated 300 cases of obesity by dietary restriction and appetite control. Appetite was best controlled by dextroamphetamine, although amphetamine and propadrine hydrochloride were found to be effective. Treatment was aimed at correcting eating habits so that the patient would have less desire for the high caloric foods. Various therapeutic agents (thyroid, ammonium chloride, salyrgan-theophylline and decholin sodium) were added successively to eliminate each refractory period. The average weight loss for the entire group for the therapy was 2 pounds (0.9 Kg.) a week. The greatest weight loss was during the first month of therapy and averaged 2½ pounds (1.1 Kg.) a week.

### American Journal of Ophthalmology, Cincinnati

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Diathermy Coagulation in Treatment of Angiomatosis Retinae and of Juvenile Coats's Disease: Report of 2 Cases. J. S. Guyton and F. H. McGovern.—p. 675.
*Colored Reflex from Anterior Capsule of Lens in Mercurialism. W. S. Atkinson.—p. 685.
Multiple Primary Malignant Neoplasms: Report of Case of Malignant Melanoma of Choroid and Glioblastoma Multiforme of Right Cerebral Hemisphere. Mary Knight Asbury and D. Vail.—p. 688.
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Abscess of Crystalline Lens. R. O. Rychener and E. C. Ellett.—p. 715.
Nevus Flammeus Associated with Glaucoma: Report of Case in Which Cyclodiathermy Was Used in an Attempt to Control Intraocular Pressure. B. Y. Alvis and Virgil A. Toland.—p. 720.
Roentgenography of Exophthalmos with Notes on Roentgen Ray in Ophthalmology. R. L. Pfeiffer.—p. 724.
Ocular Myiasis (Ophthalmomyiasis): Report of Case. R. D. Harley.—p. 742.
Bee Sting of Cornea. L. P. Glover.—p. 744.

**Colored Reflex from Lens in Mercurialism.**—Atkinson describes a brownish reflex from the anterior capsule of the lens which occurs in cases of chronic mercurialism. This reflex may be found also in those who have worked for a long time with mercury or in an atmosphere containing mercury, although

they may exhibit no symptoms of mercurialism. The reflex has not been observed in other patients nor has any previous report of such a reflex been found in the literature. This lusterless, somewhat homogeneous looking reflex from the anterior capsule of the lens is seen well with the slit lamp when a low power objective is used. When examined with oblique illumination the lenses of the eyes in which the colored reflex is pronounced present a dull gray appearance. The colored reflex, which is believed to be a deposit of mercury on or in the anterior capsule, does not disappear after the symptoms of chronic mercurialism subside or when the individual discontinues work with mercury. Some patients were examined ten and twenty years after they had last worked with mercury and the reflex was still as vivid as that which is seen in active workers who have symptoms of chronic mercurialism. Seventy persons who are or had been engaged in the manufacture of thermometers in which mercury is used were examined. One patient who had worked as a coner in the felt hat industry for over thirty years also was examined. This man exhibited definite symptoms of chronic mercurialism and a pronounced colored reflex from the anterior capsule. The colored reflex was present in 37, or over one half of the cases examined. Fourteen of the 71 manifested symptoms of chronic mercurialism, and in all of these cases the reflex was present. The author suggests that the colored reflex from the lens is a permanent and probably an early diagnostic sign of chronic mercurialism.

## American Journal of Physiology, Baltimore

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*Effect of Caffeine and Coffee Extract on Activity of Digestive Enzymes. Florence Walker.—p. 343.
Role of Brain Stem in Arterial Hypertension Subsequent to Intracranial Hypertension. F. M. Forster.—p. 347.
Observations on Circulation in Hind Limbs of Dog Ten Years Following Left Lumbar Sympathetic Ganglionectomy. H. E. Essex, J. F. Herrick, E. J. Baldes and F. C. Mann.—p. 351.
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Influence of Pregnancy, Hypervitaminosis D and Partial Nephrectomy on Volume of Parathyroid Glands in Rats. L. Opper and T. Thale.—p. 406.
Influence of Basal Forebrain Areas on Electrocorticogram. R. S. Morison, K. H. Finley and Gladys N. Lothrop.—p. 410.
Studies on Linguomaxillary Reflex. R. Greenberg and E. Gellhorn.—p. 417.
Electric Potentials of Human Small Intestine. F. M. Forster, J. D. Helm Jr. and F. J. Ingelfinger.—p. 433.

**Effect of Caffeine and Coffee Extract on Activity of Digestive Enzymes.**—Walker investigated the effect of caffeine and coffee extract on the activity of the digestive enzymes in vitro. The enzymes studied were those which act on carbohydrates, proteins and fats in the digestive tract, namely ptyalin, pancreatic amylase, pepsin, trypsin and pancreatic lipase. It was found that caffeine in concentrations of 20 mg. and 40 mg. per hundred cubic centimeters of substrate has no effect in vitro on the saccharogenic action of salivary and pancreatic amylases; nor does it affect the digestion of casein by pepsin and trypsin or of olive oil by pancreatic lipase. Coffee extract in the two concentrations studied does not affect the digestion in vitro of casein by pepsin or trypsin. It increases the rate of digestion of starch by the salivary and pancreatic amylases. It retards the digestion of olive oil by pancreatic lipase.

## American Journal of Public Health, New York

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Comparison of Nasopharyngeal Swab and Cough Plate in Diagnosis of Whooping Cough and Hemophilus Pertussis Carriers. J. J. Miller Jr., C. W. Leach, T. M. Saito and J. B. Humber.—p. 839.

**Danger of Botulism.**—According to Hall a recent tabulation shows that during the period 1899 to 1941 as many as 359 outbreaks of botulism with 1,024 cases and 669 deaths were recorded in the United States and Canada. Most of these outbreaks were caused by eating improperly home-canned vegetables. In view of the current plans of many housewives to can as much food as possible, a timely warning may help to prevent a recurrence of the catastrophic outbreaks of botulism which followed the widespread use of the "cold pack" method of home canning during the first world war. This is primarily a problem in public education of housewives and others engaged in canning and serving foods. It is recognized that while the pressure cooker, properly operated, provides the easiest and best method of home canning there is likely to be a shortage of such cookers. Correct operation should be emphasized. The author has recorded three outbreaks of botulism caused by foods supposed to have been sterilized in pressure cookers. He stresses the selection of sound produce, careful cleansing, blanching when indicated, general cleanliness, correct application of intermittent sterilization and the use of other methods of preserving food, notably drying, salting and pickling, in which there is little or no danger from botulism. With regard to consumption the author stresses the significance of turbidity, gas production, softening and odor as criteria of spoilage; the danger of eating or even tasting freshly opened home-canned foods, especially if signs of spoilage are present; the fact that certain foods, notably beets, chili, sometimes beans, and possibly other foods, may show no easily recognizable signs of spoilage even though botulinus toxin is present; the importance of the destruction of botulinus toxin by boiling home-canned foods for at least five minutes before serving; the harmlessness of the spores of Bacillus botulinus. Contaminated foods should be boiled in strong lye water to avoid killing poultry and other domestic animals, excessive pollution of the soil with the spores of Bacillus botulinus and loss of usable containers. The author stresses prompt reporting of suspicious symptoms to physicians and the saving of remnants of food for epidemiologic and laboratory studies of food poisoning.

## Anesthesiology, New York

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## Archives of Internal Medicine, Chicago

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*Clinical Experience with Mixtures of Protamine Zinc and Unmodified Insulins: Preliminary Report. Alice G. Hildebrand and E. H. Rynearson.—p. 37.
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*Symptoms and Incidence of Anemia in Hernia at Esophageal Hiatus. W. P. Murphy and W. E. Hay.—p. 58.
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Blood: Review of Recent Literature. F. H. Bethell, C. C. Sturgis, R. A. Hettig and O. T. Mallery Jr.—p. 115.

**Weil's Disease and Meningitis.**—Clapper and Myers report 13 cases of Weil's disease. In 2 both clinical and laboratory evidence of meningitis was observed; in 7 there was an abnormal cellular reaction in the cerebrospinal fluid without clinical signs of meningeal irritation, and in 1 meningismus was present without the cerebrospinal fluid showing pleocytosis. Cell counts on the cerebrospinal fluid may reach 1,000 or more per cubic millimeter. Polymorphonuclear cells predominate early and lymphocytes later. The dextrose content of the cerebrospinal fluid is not altered. Yellow discoloration of the cerebrospinal fluid is common in Weil's disease. It is at least in part due to bilirubin. Retention of urea is frequent. Pericarditis, auricular fibrillation or disturbances of conduction may occur in hearts previously normal. The plasma prothrombin, although appreciably decreased in most instances, usually does not reach levels sufficiently low to account for the hemorrhagic manifestations. Anasarca, the result of hypoproteinemia, may develop. Immunotransfusions may be of value in treatment and are worthy of a more extended trial.

**Mixtures of Protamine Zinc and Unmodified Insulins.**—According to Hildebrand and Rynearson most authors have agreed that for satisfactory control of severe diabetes mellitus protamine zinc insulin must be supplemented by unmodified insulin. The use of mixtures was first proposed by Lawrence and Aitken in 1938. At the Mayo Clinic mixtures of the two types of insulin have been used in the routine treatment of severe diabetes and proved satisfactory for a large proportion of diabetic patients. There are cases in which adequate control has been difficult and the question of adjusting the amounts of each type of insulin has not been answered. The authors studied the effects of injecting various mixtures. Observations were made on 2 young women with severe diabetes. The results of a study of the dosage of insulin in 100 cases of diabetes taken at random from the files are included. The disease in these cases was severe enough to require administration of a mixture of the two types of insulin. The authors have not been able to demonstrate that any one ratio of the protamine zinc insulin to unmodified insulin gave an optimal effect. However, ratios of protamine zinc insulin to unmodified insulin which lay between the two extremes of 1:1 and 1:5 gave the most satisfactory control; mixtures in which the ratios of protamine zinc insulin to unmodified insulin were 1:2, 1:3, 1:4, 2:3 and 2:5 were capable of adequate control of the blood sugar during the twenty-four hours after their injection. The use of a mixture of equal parts of the two insulins resulted in blood sugar curves very similar to those obtained when the dose consisted of protamine zinc insulin alone. On the other hand, a mixture of 1 part of protamine zinc insulin to 5 parts of unmodified insulin resulted in an immediate hypoglycemic effect such as might follow the injection of a large dose of unmodified insulin alone. Injection of the two types of insulins at separate sites gave not as satisfactory control of the blood sugar level as their injection together. The authors tried to eliminate the midmorning lag in hypoglycemic effect of the mixtures of the two insulins by injection of the dose of insulin one hour instead of half an hour before breakfast. Although this method eliminated the lag, it did not result in smoother control of the blood sugar during the remainder of the twenty-four hours.

**Anemia in Hernia at Esophageal Hiatus.**—Murphy and Hay attempted to determine those symptoms which may lead one to suspect the diagnosis of hiatal hernia, and to record the frequency of anemia in patients with hiatal hernia and its importance as a diagnostic aid. The data recorded are based on 72 histories of patients with hiatal hernia, of whom 11 were men and 61 women. Hiatal hernia is more common in female patients. The average age was 60 years. Seven of this series had a congenitally short esophagus. Six of them were troubled with vomiting or regurgitation after ingestion of food. Substernal pain, distress or a feeling of obstruction in this location was present in 5 of these patients. Obesity is an important contributory factor to hiatal hernia. Increased intra-abdominal pressure, which may be produced by excess fat in the omentum, a large fibroid or a pregnant uterus, may cause herniation. Rigler emphasized the importance of pregnancy as a factor. Slightly more than one half of this series were women who had been pregnant one or more times. Trauma is undoubtedly responsible in some cases. Pain was the symptom most frequently stressed by the patients. Anemia rates second to pain in order of frequency. Other symptoms were vomiting, nausea, gas in the stomach, fatigability, diarrhea, heartburn, constipation, anorexia, headache and indigestion. A characteristic his-

tory is as follows: After the ingestion of food, particularly solid or coarse, there is a feeling of obstruction or pain (ache or squeeze) in the substernal or the upper epigastric region. This may be followed by regurgitation or vomiting, with relief of symptoms. Vomiting and regurgitation of food not associated with nausea are characteristic complaints. Hiatal hernia should be more frequently included in the differential diagnosis of pathologic conditions in the upper part of the abdomen. An analysis of the blood was made in 67 of this series. A diagnosis of pernicious anemia was made in 7. In 2 other cases there was severe macrocytic anemia with a high color index. If one excludes the 7 patients with pernicious anemia, there were 40, or 66 per cent, with anemia of some degree. Anemia is so commonly associated with hiatal hernia that it must be considered an important aid in the diagnosis. It is usually hypochromic and the result of hemorrhage arising from ulceration of the esophageal or of the gastric mucosa or from congestion of the mucous surfaces. Surgical intervention may be necessary in hiatal hernia, particularly when there is incarceration of the stomach in the esophageal hiatus with symptoms of obstruction and recurrence of severe hemorrhage. Medical management should include a diet low in roughage, with avoidance of solid foods; later the diet should be increased to include some moderately rough and coarse foods. It may include puréed vegetables. It should be divided into five or six small meals daily. At no time should the stomach be overloaded. Loss of weight will be desirable in the obese. Patients should rest before meals. The patient should not recline soon after a meal. Those whose symptoms occur at night or on reclining will be benefited by sleeping in a semireclining position. The patient should be cautioned against lifting heavy objects or lifting any object from a bending over position. All straining and physical effort should be avoided. The hypochromic anemia should be treated with optimal doses of iron.

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Congenital Paralysis of Lateral Rotators of Eyes with Paralysis of Muscles of Face. A. M. Hicks.—p. 38.
Absorption of Infra-Roentgen (Bucky) Rays of Various Qualities by Anterior Portions of Eyeball. F. Sagher and E. Sagher.—p. 43.
Association Between Aniseikonia and Anomalous Binocular Space Perception. K. N. Ogle.—p. 54.
*Local Toxic Effects of Sulfanilamide and Some of Its Derivatives. J. G. Bellows, with laboratory assistance of R. Gluckman.—p. 65.
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Intraocular Hemorrhages in Choline Deficiency. J. G. Bellows and H. Chinn.—p. 105.
Bacteriologic Observations in Infections of Eye. C. Weiss.—p. 110.

**Local Toxic Effects of Sulfonamide Compounds.**—Bellows investigated the effects of local application of the sulfonamide drugs on the eyeball. The corneas of young adult rabbits were anesthetized by means of a 4 per cent cocaine hydrochloride solution, which was chosen not only for its anesthetic properties but for its drying effect on the epithelium. The drying effect was desired because it facilitated removal of the epithelium, an operation which was accomplished by immobilization of the eyeball with a fixation forceps and rubbing of the cornea with dry gauze. The cornea was stained with fluorescein to make certain that the epithelium was completely removed. Sulfanilamide, sulfathiazole, sulfapyridine and sulfadiazine were used in the form of powder, a 5 per cent ointment and a 20 per cent suspension. The drug to be tested was applied three times daily to one eye, while the other eye served as a control. These experiments yielded additional support to the contention that the sulfonamide compounds have an unfavorable effect on actively growing epithelium as shown by a greater than twofold increase in the time required for epithelial regeneration. They increase the amount of scarring. Therefore the local use of these drugs should be avoided in the treatment of injuries of the face or cornea.

## Arkansas Medical Society Journal, Fort Smith

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Treatment and Rehabilitation of Hard of Hearing Child. J. K. Leasure.—p. 391.
The Sulfonamides. F. F. Yonkman.—p. 394.

**Intradermal Vaccine Therapy in Brucellosis.**—According to Urschel intradermal injection of brucella vaccine or brucellergen causes the development of specific antibodies in the blood stream of the patient. The significance of these demonstrable antibodies in resistance to infection has not been demonstrated. In a small series of cases vaccine given by the intradermal route has given satisfactory clinical response. A mixed heat-killed stock vaccine was used. After the diagnosis has been made, treatment is begun with intradermal injections at five to seven day intervals (in an occasional case at three to five day intervals). The vaccine is injected into the forearm or into the medial surface of the thigh. Twenty intradermal injections of vaccine was the average in this group. Twenty-eight patients have received treatment by intradermal vaccine alone and three have had a combination of intradermal and subcutaneous vaccine. In 87.5 per cent of patients the intradermal administration of vaccine alone got results which were classified as fair, good or excellent. The intradermal route offers several advantages. The amount of vaccine necessary is small. The injections are relatively painless. The amount of reaction can be carefully watched and measured. Systemic reactions are few.

**Succinylsulfathiazole in Chronic Brucellosis.**—Davis suggests that an intestinal antiseptic might solve the therapeutic problem of involvement of the digestive tract in patients with brucellosis. Since September 1942 the author has used succinylsulfathiazole for all patients with chronic brucellosis. To date he has used this drug in the treatment of 18. Ten patients are apparently cured, 6 are much improved but still under treatment, and 2 have up to the present time shown no response to the drug. The author is unable to give any explanation of the two failures.

## Iowa State Medical Society Journal, Des Moines

**33**:295-368 (July) 1943

Public Opinion and Professions. V. M. Hancher.—p. 295.
Intraocular Neuritis. E. C. Montgomery.—p. 298.
Public Health Today. F. J. Underwood.—p. 301.
Barbiturate Poisoning. J. W. Lawrence.—p. 303.

**33**:369-408 (Aug.) 1943

Pelvic Surgery as Related to General Practice. V. S. Counseller.—p. 369.
*Malaria Endemic in Iowa. A. W. Bennett.—p. 372.
Kenny Treatment in Acute Poliomyelitis: Report of First Year at Iowa Lutheran Kenny Cottage. J. E. Dyson.—p. 375.
Mitral Endocarditis and Coronary Thrombosis. F. P. McNamara.—p. 379.

**Malaria in Iowa.**—Bennett reports 4 cases of malaria. The histories indicated that the onset occurred the same day. The prodromal symptoms were similar: Each patient had the initial chill, which was severe and prolonged and was followed by temperatures reaching from 104 to 105 F. with subsequent sweats and weakness. The four persons had met at a picnic in a lake resort. They recalled that the mosquitoes had been plentiful. It seems possible that the inoculation occurred at this time. It is not clear where the mosquito or mosquitoes became infected. Two sources seem probable: Lake McBride is a state park and many people from a distance visit it. Some one who previously had had malaria and was a carrier might have visited there and the mosquito or mosquitoes fed on him and thus became infected. The other possible source is that in many medical centers, among them the State University of Iowa Hospital, certain patients are routinely treated with malarial inoculations. A strain of Plasmodium vivax is used for this purpose; the same strain was detected in these patients. The treatment of malaria proved difficult. During the initial attack these patients were all treated promptly and energetically with quinacrine and quinine as soon as the diagnosis was confirmed by blood findings. During each of the following relapses they were treated with quinacrine, plasmochin and quinine. Each had from three to four recurrences, all verified by finding the parasite in the blood smears.

## Journal of Bone and Joint Surgery, Boston

**25**:503-730 (July) 1943

Correlation of Clinical and Anatomic Facts Leading to Conception of Etiology of Congenital Hip Dysplasias: President's Address. C. E. Badgley.—p. 503.
Some Surgical Lessons of War. W. R. Bristow.—p. 524.
Treatment of Difficult and Unusual Nonunions, with Special Reference to Bridging of Defects. H. B. Boyd.—p. 535.
Bone Changes in Acute and Chronic Scurvy: An Experimental Study. S. W. Banks.—p. 553.
Importance of Leaving a Good Amputation Stump. A. B. Lemesurier.—p. 566.
Use of Cellophane as Interposition Membrane in Synovectomy. D. C. McKeever.—p. 576.
Paralytic Scoliosis. A. Farkas.—p. 581.
Etiology of Undescended Scapula and Related Syndromes. D. Engel.—p. 613.
Stabilization of Articulation of Greater Multangular and First Metacarpal. D. B. Slocum.—p. 626.
Pin Distraction as Cause of Nonunion. A. G. Davis.—p. 631.
Experimental Uses of Sulfonamides and Other Drugs in Acute Purulent Arthritis. C. J. Frankel and N. W. Larkum.—p. 644.
Kenny Treatment for Infantile Paralysis: Comparison of Results with Those of Older Methods of Treatment. R. Bingham.—p. 647.
Recurrent Dislocation of Shoulder Joint: Combination Procedure; Preliminary Report. F. W. Ilfeld and H. G. Holder.—p. 651.
Choice of Anesthetic Agent and Care of Patient in Relation to Anesthesia in Orthopedic Surgery. J. Lyford.—p. 659.
Care of Knee Following Excision of Meniscus. S. R. Terhune, T. S. Eddleman, S. B. Thompson and B. S. Read.—p. 663.
Fractures of Neck of Metacarpal. I. Redler.—p. 670.
*Etiology and Surgical Treatment of Intractable Pain About Fourth Metatarsophalangeal Joint (Morton's Toe). R. T. McElvenny.—p. 675.
Self-Adjusting Foot Piece for Preventing or Correcting Equinus Deformity When Traction is Applied to Lower Extremity. L. D. Baker and F. J. Reed.—p. 680.

**Pain in the Fourth Metatarsophalangeal Joint (Morton's Toe).**—According to McElvenny a typical case of Morton's toe is characterized by severe lancinating pain originating in the region of the fourth metatarsophalangeal joint. The pain is shooting in character and may travel up the calf as far as the knee. The pain comes on in paroxysms of varying intensity and in many subjects is accompanied by an almost uncontrollable desire of the victim to remove the shoe. The disease occurs in men and in women in the proportion of about six to ten. This condition was first described by Morton of Philadelphia in 1876. The condition is often resistant to conservative treatment. It is caused by a tumor involving the most lateral branch of the medial plantar nerve. Careful palpation will usually reveal the tumor, which lies high in the web between the third and fourth toes. If symptoms justify it, excision of the tumor should be done. The author reports 11 cases treated by operation. Of the twelve tumors removed from 11 patients, five have had a microscopic study and appear to be either neurofibromas or angioneurofibromas. Grossly they are fatty and soft on the outside and firm, white and fibrous as the center is approached. The plantar nerve is embedded in the center.

## Journal of Clinical Investigation, Boston

**22**:471-634 (July) 1943

Relationship of Dehydration and Overhydration of Blood Plasma to Collapse in Management of Artificial Fever Therapy. H. R. Brown Jr., W. F. Clark, N. Jones, Johanna Walther and S. L. Warren.—p. 471.
Fractionation of Serum and Plasma Proteins by Salt Precipitation in Infants and Children: 1. Changes with Maturity and Age. 2. Changes in Glomerulonephritis. 3. Changes in Nephrosis. M. Rapoport, M. I. Rubin and D. Chaffee.—p. 487.
Prolongation of Action of Subcutaneously Injected Medicines in Man. F. F. Foldes.—p. 499.
Effect of Opiates on Pain Threshold in Post Addicts. H. L. Andrews.—p. 511.
Skin Resistance Changes and Measurements of Pain Threshold. H. L. Andrews.—p. 517.
Study of Volume of Blood in Congestive Heart Failure: Relation to Other Measurements in 15 Patients. G. R. Meneely and N. L. Kaltreider.—p. 521.
Quantitative Relationship Between Basal Metabolic Rate and Thyroid Dosage in Patients with True Myxedema. A. W. Winkler, J. Criscuolo and P. H. Lavietes.—p. 531.
Tolerance to Oral Thyroid and Reaction to Intravenous Thyroxine in Subjects Without Myxedema. A. W. Winkler, P. H. Lavietes, C. L. Robbins and E. B. Man.—p. 535.
Electrophoretic and Chemical Analysis of Protein in Nephritic Urine. S. S. Blackman Jr. and B. D. Davis.—p. 545.
Defect in Metabolism of Tyrosine and Phenylalanine in Premature Infants: III. Demonstration of Irreversible Conversion of Phenylalanine to Tyrosine in Human Organism. S. Z. Levine, Margaret Dann and Eleanor Marples.—p. 551.
Relation of Cephalin Flocculation and Colloidal Gold Reactions to Serum Proteins. E. A. Kabat, F. M. Hanger, D. H. Moore and H. Landow.—p. 563.
Studies Regarding a Glutamine-like Substance in Blood and Spinal Fluid, Including a Method for Its Quantitative Determination. M. M. Harris, with technical assistance of Roslyn T. Roth and Ruth S. Harris.—p. 569.
Effect of Insulin Hypoglycemia and Glucose Administration on Level of Glutamine-like Substance in Blood Serum. M. M. Harris with technical assistance of Roslyn T. Roth and Ruth S. Harris.—p. 577.
Effect of Testosterone and Allied Compounds on Mineral, Nitrogen and Carbohydrate Metabolism of Girl with Addison's Disease. N. B. Talbot, A. M. Butler and E. A. MacLachlan.—p. 583.
Mode of Excretion of Creatine and Creatinine Metabolism in Thyroid Disease. N. A. Tierney and J. P. Peters.—p. 595.
Locus Action of Parathyroid Hormone: Experimental Studies with Parathyroid Extract on Normal and Nephrectomized Rats. T. H. Ingalls, G. Donaldson and F. Albright.—p. 603.
Treatment of Burns by Closed Plaster Method, with Certain Physiologic Considerations Implicit in Success of This Technic. W. W. L. Glenn, Helen H. Gilbert and C. K. Drinker.—p. 609.
Changes in Electrophoretic Pattern in Lymph and Serum in Experimental Burns. G. E. Perlmann, W. W. L. Glenn and D. Kaufman.—p. 627.

## Journal of Experimental Medicine, New York

**78**:1-90 (July) 1943

Antigenic Properties of Native and Regenerated Horse Serum Albumin. J. O. Erickson and H. Neurath.—p. 1.
Synergistic Action of Hemophilus Influenzae Suis and Swine Influenza Virus on Chick Embryo: II. F. B. Bang.—p. 9.
Influence of Age of Host and Temperature of Incubation on Infection of Chick Embryo with Vesicular Stomatitis Virus. B. Sigurdsson.—p. 17.
Studies on Site of Antibody Formation in Rabbits Following Intracutaneous Injections of Pneumococcus or of Streptococcus Vaccine. P. F. DeGara and D. M. Angevine.—p. 27.
Hypotension and Loss of Pressor Response to Angiotonin as Result of Trauma to Central Nervous System and Severe Hemorrhage. I. H. Page.—p. 41.
Studies in Sensitization to Skin: I. Production of Antibodies to Skin by Means of Synergistic Action of Homologous Skin Antigen and Staphylococcus Toxin. R. Hecht, M. B. Sulzberger and H. Weil.—p. 59.
Studies on Experimental Hypertension: XXI. Purification of Renin. Y. J. Katz and H. Goldblatt.—p. 67.
Metabolism of Ischemic Kidney: I. Respiration and Oxidase Activity of Ischemic Kidney. S. B. Raska.—p. 75.

## Journal of Immunology, Baltimore

**46**:347-504 (June) 1943

Immunochemistry of Allergens: II. Antigenic Studies by Dale Method of Electrophoretic Fractionation Products of Protein-Carbohydrate Fraction CS-1A from Cottonseed. E. J. Coulson, J. R. Spies and H. Stevens.—p. 347.

Id.: III. Anaphylactogenic Potency of Electrophoretic Fractionation Products of CS-1A from Cottonseed. E. J. Coulson and J. R. Spies.—p. 367.

Id.: IV. Effect of Dilute Acid on Anaphylactogenic Activity, Specificity and Reagin Neutralization Capacity of Cottonseed Allergenic Fractions. E. J. Coulson and J. R. Spies.—p. 377.

Evaluation of Antigenicity of Tetanal Toxoid. W. L. Koerber.—p. 391.

Cross Protection Between Heterologous Agglutinogenic Types of Beta Hemolytic Streptococci of Group A: II. An Immunogenic Group of Four Types. Alice C. Evans.—p. 399.

Use of Mice in Testing of Antigenic Power of Tetanal Toxoid. W. L. Koerber and Gertrude E. Mook.—p. 411.

Studies of Antipneumococcal Serum: IV. Maximally Reactive Proportions of Antigen and Antiserum in Precipitation and Complement Fixation. Christine E. Rice.—p. 427.

State of Salmonella Problem. S. Bornstein.—p. 439.

## Journal of Lab. and Clinical Medicine, St. Louis

**28**:1175-1294 (July) 1943

Verification Test in Serology of Syphilis. R. L. Kahn.—p. 1175.

Production of Chronic Hypertension in Dogs by Progressive Ligation of Arteries Supplying the Head. H. R. Fishback, F. E. Dutra and E. T. MacCamy.—p. 1187.

Human Skin as Conductor of 60 Cycle Alternating Current of High Intensity, Studied on "Electroshock" Patients. H. Lōwenbach and J. E. Morgan.—p. 1195.

Some New Aspects of Morphine Action: Influence of Prostigmine Methylsulfate on Excretion. D. Slaughter, C. R. Treadwell and J. W. Gales.—p. 1199.

Immunologic and Toxic Properties of Casein Digest as Prepared for Parenteral Administration. H. C. Hopps and J. A. Campbell—p. 1203.

*Caffeine Withdrawal Headache. R. H. Dreisbach and C. Pfeiffer.—p. 1212.

Etiology of Migraine Syndrome—Physiologic Approach. C. Pfeiffer, R. H. Dreisbach, C. C. Roby and H. G. Glass—p. 1219.

Chronic Brucellosal Type of Ankylosing Spondylitis. E. Goldfain.—p. 1226.

Significance of Gross Character of Sputum in Prognosis of Pneumococcic Pneumonia. A. W. Frisch, A. E. Price and G. B. Myers.—p. 1231.

Comparative Accuracy of Closed Circuit Bedside Method and Open Circuit Chamber Procedure for Determination of Basal Metabolism. R. C. Lewis, Alberta Iliff and Anna Marie Duval.—p. 1238.

**Caffeine Withdrawal Headache.**—Dreisbach and Pfeiffer attempted to produce and study caffeine withdrawal headache. In a survey of 128 migraine patients 25 stated that lack of their usual coffee intake would result in headache. Five patients volunteered the information that the headache was not of the migraine type. The authors attempted to produce headache by administration of caffeine over a suitable period, usually a week, and then abruptly withdrawing the drug. In 55 per cent of thirty-eight trials on 22 subjects, headache as extreme in severity as the subjects had ever experienced was produced by the sudden withdrawal of caffeine. In 29 per cent of the trials the headache was definite but did not require treatment. In 16 per cent of the experiments little or no headache resulted. The headache is without scotomas, slow in onset and central in origin, becoming generalized after four to six hours; it may be accompanied by nausea and vomiting. In migraine subjects the headache differs from their typical migraine headache. The blood studies indicate that a lowered serum calcium, an elevated serum phosphorus and possibly an increase in blood volume accompany the headache.

## Journal-Lancet, Minneapolis

**63**:193-224 (July) 1943

*Rocky Mountain Spotted Fever: Nine Year Study of Wyoming Cases. G. E. Baker.—p. 207.

War Wounds of Abdomen. D. L. Borden.—p. 213.

Practical Problems in Blood Grouping and Blood Transfusion. R. F. Peterson.—p. 215.

**Rocky Mountain Spotted Fever.**—Baker points out the close resemblance of endemic typhus to Rocky Mountain spotted (tick) fever. The degree of protection afforded by vaccine and the duration of such protection vary. As a rule those vaccinated in the spring of the year retain a considerable degree of immunity for at least the remainder of that year. Treatment of tick fever is purely symptomatic and supportive in character. Bed rest with good nursing care is necessary. The author had occasion to study the various aspects of tick fever in a section of Wyoming where the disease occurs with considerable frequency. In 1934 Kamp and the writer received encouraging reports of responses obtained in typhus by use of neoarsphenamine dissolved in aqueous solution of metaphen. In the spring and summer of 1934 they used this treatment in 9 moderately severe cases of the disease. None of the patients succumbed to their illness. Since that time an average of 3 to 4 cases of tick fever have been under the writer's care each season. During the past eight years recovery has occurred in all cases so treated. A combination of the bactericidal action of metaphen, together with the spirocheticidal action of neoarsphenamine, on a micro-organism which is bacterium-like in character yet has staining properties similar to those displayed by spirochetes may be the secret of the success. In this treatment 0.3 Gm. of neoarsphenamine was dissolved in 10 cc. of an aqueous solution of 1:1,000 metaphen. The mixture was warmed and injected slowly into a vein. Administration is repeated at three or four day intervals. Three or four injections have customarily been sufficient to ameliorate the clinical picture so as to insure ultimate recovery. Should severe renal injury exist as a result of the infection, careful consideration must then be given the question as to whether the use of these medicaments is justified.

## Journal of Nutrition, Philadelphia

**26**:1-104 (July) 1943

Further Studies on Symptoms of Manganese Deficiency in Rat and Mouse. M. E. Shils and E. V. McCollum.—p. 1.

Role of Dietary Protein in Hemoglobin Formation. Aline Underhill Orten and J. M. Orten.—p. 21.

Effect of Concentration on Absorption of Vitamin A. A. G. Reifman, Lois F. Hallman and H. J. Deuel Jr.—p. 33.

Nutritive Differences in Rations Containing Unhydrogenated or Hydrogenated Fats as Shown by Rearing Successive Generations of Rats. H. G. Miller.—p. 43.

Amino Acids Required for Growth in Mice and Availability of Their Optical Isomers. C. D. Bauer and C. P. Berg.—p. 51.

Biotin Content of Meat and Meat Products. B. S. Schweigert, E. Nielsen, J. M. McIntire and C. A. Elvehjem.—p. 65.

*Retention of Vitamins in Meats During Storage, Curing and Cooking. B. S. Schweigert, J. M. McIntire and C. A. Elvehjem.—p. 73.

Studies of Calcium and Phosphorus Metabolism in Chick: I. Comparative Effect of Vitamins $D_2$ and $D_3$ and Dihydrotachysterol Given Orally and Intramuscularly. E. W. McChesney.—p. 81.

Vitamin K and Prothrombin Levels with Special Reference to Influence of Age. F. W. Stamler, R. T. Tidrick and E. D. Warner.—p. 95.

**Vitamins in Meat During Storage, Curing and Cooking.**—For the experiments carried out by Schweigert and his associates pork hams were taken from carcasses weighing approximately 190 pounds. Paired hams were used throughout the experiment. Two fresh hams were analyzed immediately and the two corresponding hams were stored for fourteen days in a freezer (—4 C.) in order to determine the vitamin retention during storage. Two different hams were stored for fourteen days and the corresponding two hams were cured commercially in order to study vitamin retention during the curing process. Four additional hams were cured. Two of these were analyzed uncooked and the two corresponding hams were used for cooking tests. The authors found that average retention during storage is 92 per cent for the thiamine and nicotinic acid and 85 per cent for the riboflavin. The retention in curing was found to be 73 per cent for the thiamine, 84 per cent for the nicotinic acid and 92 per cent for the riboflavin. The average retention in the meat alone after roasting was 58 per cent for thiamine, 79 per cent for the nicotinic acid and 74 per cent for the riboflavin; after frying, 86 per cent for the thiamine, 85 per cent for the nicotinic acid and 77 per cent for the riboflavin. The average total retention in the meat plus drippings after roasting was 70 per cent for thiamine, 96 per cent for the nicotinic acid and 84 per cent for the riboflavin; after frying, 92 per cent for the thiamine, 96 per cent for the nicotinic acid and 86 per cent for the riboflavin. The over-all retention of the vitamins from fresh stored to cured fried samples agrees very well with the vitamin retention during curing and frying. From 10 to 15 per cent of each of the vitamins was found in the drippings from roasting and frying. A higher retention of thiamine in the meat alone was found after frying, as compared with roasting, braising and broiling.

## Journal Pharmacology & Exper. Therap., Baltimore

**78**:215-320 (July) 1943

Effect of Sodium Diphenyl Hydantoinate (Dilantin Sodium) on Utilization of Ascorbic Acid by Guinea Pigs. A. D. Emmett, Eva R. Hartzler and R. A. Brown.—p. 215.
Studies on Chemistry and Pharmacology of Melanophore Hormone of Pituitary Gland. G. Chen and E. M. K. Geiling.—p. 222.
Studies on Veratrum Alkaloids: III. Qualitative and Quantitative Differences in Action of Cevine and Veratridine. R. Mendez and G. Montes.—p. 238.
Chronic Selenium Poisoning in Dogs and Its Prevention by Arsenic. M. Rhian and A. L. Moxon.—p. 249.
Didhydroxypropyl Bismuthate: Experimental Studies of New Bismuth Compound. L. M. Wheeler.—p. 265.
*Effect of Cholesterol Administration on Anesthesia. F. F. Foldes and H. K. Beecher.—p. 276.
Treatment of Standardized and Graded Histamine Shock in Dogs with Solutions of Methyl Cellulose and S-Methylisothiourea Sulfate. W. C. Hueper and C. T. Ichniowski.—p. 282.
Narcosis Induced by Carbon Dioxide at Low Environmental Temperatures. J. H. Barbour and M. H. Seevers.—p. 296.
Stimulating Action of Colchicine on Pituitary Induced Ovulation of Frog. M. K. McPhail and K. M. Wilbur.—p. 304.
Studies on Antimalarial Drugs: Distribution of Quinine in Tissues of Fowl. F. E. Kelsey, Frances K. Oldham and E. M. K. Geiling.—p. 314.

**Effect of Cholesterol Administration on Anesthesia.**—Foldes and Beecher were able to confirm for ether and a barbiturate the principal conclusion of Starkenstein and Weden that the depth and duration of anesthesia can be greatly increased by the previous injection of cholesterol. The cholesterol effect appears to be a potentiation; the possibility that it may be additive cannot be eliminated at this time. In searching for an explanation of the cholesterol action one must look beyond physical solubility and transport effects: (*a*) Both olive oil and cholesterol increase the effectiveness of ether, but only cholesterol increases the effectiveness of the barbiturate. Olive oil has no effect on the barbiturate. (*b*) Ether has the same order of solubility in both cholesterol and lecithin: yet cholesterol increases the anesthetic effect of ether (and barbiturate) while lecithin does not.

## Missouri State Medical Assn. Journal, St. Louis

**40**:191-240 (July) 1943

Plans for Postwar Medical Service. M. Fishbein.—p. 191.
Value of Strophanthin in Coronary Disease. R. Uhlmann.—p. 194.

**40**:241-268 (Aug.) 1943

More Extensive Operation for Hypertension: Report of Cases. R. M. Klemmer and R. D. Woolsey.—p. 241.
Uses and Abuses of Sulfa Drugs. R. O. Muether.—p. 245.

## New England Journal of Medicine, Boston

**229**:33-96 (July 8) 1943

Physiologic Considerations in Treatment of Nephritis. G. W. Thorn.—p. 33.
Meningococcal Meningitis with Purulent Arthritis: Report of Case. J. P. Cattell.—p. 49.
Clinical Catalytic Chemistry. W. T. Salter.—p. 53.

**229**:97-132 (July 15) 1943

*Thiouracil in Treatment of Thyrotoxicosis. R. H. Williams and G. W. Bissell.—p. 97.
Spina Bifida and Cranium Bifidum: V. Arnold-Chiari Malformation; Study of 20 Cases. F. D. Ingraham and H. W. Scott Jr.—p. 108.
Modification of Intestinal Motility by Drugs. F. J. Ingelfinger.—p. 114.

**Thiouracil in Treatment of Thyrotoxicosis.**—Recently substances have been described which induce goiter presumably by their direct action on the thyroid. Such substances are the sulfonamides, thiourea and thiourea derivatives. Following their administration to certain animals, particularly rats, thyroid enlargement results in a few days. Microscopically, one finds hyperplasia of the acinar cells and a decrease in the colloid of the follicles. A drop in the basal metabolic rate occurs. These changes can be prevented by the administration of desiccated thyroid or thyroxin. They can also be prevented by hypophysectomy but not by the administration of iodine. In rats fed sulfaguanidine, changes in the pituitary glands similar to those following thyroidectomy take place. These facts suggest that the drugs act directly on the thyroid gland, inhibiting the production of thyroxin, this in turn leading to a decrease in the body metabolism and to an increased activity of the pituitary gland. The authors have been studying some of the pharmacologic and therapeutic effects of thiouracil in patients with thyrotoxicosis. None of the patients were given iodine. Thiouracil was given by mouth, usually in doses of 0.2 Gm. The authors give detailed histories of 9 unselected patients with thyrotoxicosis whom they treated with thiouracil. In each case the toxic manifestations disappeared and the basal metabolic rate returned to a normal range. Blood iodine studies conducted on 4 patients showed in each a fall of the protein bound iodine to a low normal or subnormal level. Studies have been performed of the blood levels of thiouracil and its excretion in the urine. No serious complications from the drug have been encountered, but all patients receiving the drug should be carefully followed. This report deals only with the early changes resulting from the treatment with thiouracil.

**229**:133-190 (July 22) 1943

Oliver Wendell Holmes and Puerperal Fever. F. C. Irving.—p. 133.
Care of Victims of Cocoanut Grove Fire at Massachusetts General Hospital. O. Cope.—p. 138.
Gastrointestinal Symptoms of Heart Disease. L. M. Hurxthal.—p. 148.
Orthopedic Surgery. W. A. Rogers.—p. 152.

**229**:191-228 (July 29) 1943

*Diaphragmatic (Hiatus) Hernia: Clinical Study. W. R. Ohler and M. Ritvo.—p. 191.
Acute Laryngotracheobronchitis in Children. J. A. V. Davies.—p. 197.
Diagnosis of Virus and Bacterial Pneumonia in Children. M. Finland.—p. 199.
Use of Sulfonamides in Treatment of Respiratory Infections in Children. C. A. Janeway.—p. 201.
Lateral View in Roentgenologic Diagnosis of Lesions of Colon. E. G. Wissing and R. M. Lowman.—p. 207.
Orthopedic Surgery (concluded). W. A. Rogers.—p. 211.

**Diaphragmatic (Hiatus) Hernia.**—Ohler and Ritvo collected from the records of the Boston City Hospital 128 cases of diaphragmatic (hiatus) hernia during a period of less than four years. They conclude that the condition is not rare. The symptoms are such as to justify its inclusion in the differential diagnosis of anterior chest or upper abdominal complaints or both. The typical symptom of hiatus hernia is a sense of epigastric pain, distress and fulness coming on shortly after or during meals. Often there is difficulty in swallowing solid food. Frequently there is epigastric pain or distress at night or when the patient is in the recumbent position. In most cases the pain is relieved when the patient assumes the upright position. There may be substernal pain or dyspnea or both—generally but not always unrelated to exertion. The pain may present radiation similar to that of angina pectoris, but just as frequently its radiation is atypical. The patient with hiatus hernia may bleed. The bleeding may explain the anemia characteristic of chronic blood loss. The x-ray examination should always begin with fluoroscopic observations without the opaque meal. A careful search is made for a gas containing shadow lying at or slightly above the level of the diaphragm. This is of particular importance, since in some cases the hernia reduces itself and disappears on ingestion of the opaque meal. Observations are first made with the patient breathing quietly, then in full inspiration and forced expiration. The frontal and oblique positions are used in the erect, prone and supine positions. When the opaque meal is administered, the fluoroscopic observations are best begun with the patient in the erect position. The great majority of hernias are not demonstrable in this position. The lesion will not be visualized if the x-ray observations are carried out only with the patient upright. Treatment is essentially medical, especially in patients with small lesions. A bland, high vitamin diet, divided into four or six feedings, is desirable. Food should not be given before bedtime. Assumption of the upright position after eating or for a few minutes during the course of the meal is often helpful. Sleeping at an angle of 45 degrees has relieved distressing night symptoms. Alkalis and antispasmodic drugs are frequently useful. Surgery is indicated when medical measures fail, especially for patients having intractable pain or hemorrhagic tendencies.

## New Jersey Medical Society Journal, Trenton

**40**:213-256 (June) 1943

Plasma and Blood Banks in Wartime. E. M. Katzin.—p. 218.
Stricture of Rectum. F. C. Yeomans.—p. 222.

**40**:257-296 (July) 1943

Opiferque per Orbem Dicor: Presidential Address. E. J. Marsh. —p. 260.
Essential Procedures in Immediate Care of Fresh Major Traumatic Wounds. J. M. Carlisle.—p. 263.
Tuberculosis in Wartime and After. E. Frankel.—p. 266.
Traumatic Epilepsy: Pathologic Factors. K. W. Ney.—p. 270.
Pregnancy and Labor Complicated by Heart Disease. B. Tunis. —p. 276.

## Northwest Medicine, Seattle

**42**:151-178 (June) 1943

Psychoneuroses of War: Care of Ill and Injured After Evacuation from Combat Zones. K. M. Bowman.—p. 154.
Military Mental Conservation and Rehabilitation. N. K. Rickles. —p. 158.
Medical Civilian Practice in Wartime. J. E. Hunter.—p. 160.
Surgical Practice in Wartime. E. A. Nixon.—p. 161.
Medical Service in Industry. H. J. Whitacre.—p. 163.
War Civilian Security Program. C. M. Smith.—p. 165.
Endemic and Epidemic Diseases: Including Tropical Disease. T. B. H. Anderson.—p. 167.

**42**:179-206 (July) 1943

Control of Blood Coagulability with Coumarin and other Drugs. J. E. Rhoads, J. Walker and Lillian Panzer.—p. 182.
Surgical Experiences with Malignant Tumors. J. W. Baker.—p. 186.
Nonunion of Femoral Neck Fractures. L. H. Edmunds.—p. 190.
Endometrioma of Sigmoid. R. S. Smith.—p. 192.
Functional Supernumerary Mammary Glands. J. V. Schwind.—p. 195.
Administration of Histamine in Allergic Conditions. W. N. M. Girling. —p. 196.
Meningococcic Meningitis. P. V. Woolley and T. Parry.—p. 197.

## Ohio State Medical Journal, Columbus

**39**:609-704 (July) 1943

Nutrition and Child Health. A. A. Weech.—p. 625.
Industrial Absenteeism: Its Medical Phase. R. F. Jukes.—p. 629.
History and Incidence of Rabies. E. R. Shaffer.—p. 631.
Diagnosis, Treatment and Prevention of Chigger Bites. H. J. Parkhurst.—p. 639.
Allergy to an Estrogen: Dermatosis from Estradiol-17 Carbethoxyate. R. D. Barnard.—p. 642.
Significance of Rh Factor in Intragroup Transfusion Reactions and Erythroblastosis Fetalis: Report to Physician in Practice. A. P. Falkenstein.—p. 644.
Misconceptions Concerning Peripheral Vascular Diseases. D. M. Palmer.—p. 647.
Role of Aluminum in Nutrition. J. Forman.—p. 651.
Addison's Disease Due to Cytotoxic Contraction of Adrenal Cortex with Sudden Death Four Days After Appendectomy. T. C. Laipply. —p. 652.

## Oklahoma State Medical Assn. Jour., Oklahoma City

**36**:231-276 (June) 1943

Medical Management of Diseases of Gallbladder and Biliary Tract. F. C. Rewerts.—p. 231.
Simplified Treatment for Impetigo Neonatorum. C. E. White.—p. 234.
Treatment of Burn Cases off the U. S. S. Wasp. R. G. Jacobs.—p. 235.
Consideration of Kenny Treatment of Infantile Paralysis. D. H. O'Donoghue.—p. 236.
Private Practitioner and War Industry. D. H. Macrae.—p. 239.

**36**:277-322 (July) 1943

Spontaneous Pneumothorax in Apparently Healthy Young Adults. J. F. Moorman.—p. 277.
*Rocky Mountain Spotted Fever. P. Sizemore.—p. 282.
Plasma Bank. A. R. Wiley.—p. 285.
Neuropsychiatric Problems Arising in Civilian Population. J. A. Willie. —p. 287.

**Rocky Mountain Spotted Fever.**—Sizemore reports observations in 7 cases of Rocky Mountain spotted fever. The cases occurred in a family in the town of Armstrong in Bryan County, which is located in the south central section of Oklahoma. The family lived here for several years but had moved into a new, unpainted, green lumber house only a short distance from their previous home. The household consisted of a couple, their 3 children and the wife's mother. The latter, aged 67, died of the illness contracted by all of them. All developed what was first suspected to be typhus but later was identified as Rocky Mountain spotted fever. The attending physician, Dr. Flythe, aged 44, died of the disease. A man aged 47 who had stayed at the home of the family while the first 3 members were ill became ill and died. The rash suggested that this fatality was also caused by the Rocky Mountain spotted fever. Questioning brought out the fact that all members of the household had been bitten repeatedly since moving to the new house by ticks which infested the yard. The gopher proved to be the ticks' host in the Armstrong area. The use of vaccine in infested areas each year is indicated. This is best given in late winter or early spring. The vaccination should be completed at least ten days before the first expected exposure. The vaccine is not recommended for therapeutic use.

## Pennsylvania Medical Journal, Harrisburg

**46**:1009-1120 (July) 1943

Summary of Endocrine Effects in Advanced Prostatic Cancer. C. B. Huggins.—p. 1023.
Clinical Observations on Estrogenic Therapy in Prostatic and Bladder Carcinoma and Benign Prostatism. W. H. Haines and S. Miceli. —p. 1025.
Testosterone Therapy in Male Hypogonadism. J. F. McCahey.—p. 1029.
Importance of Wheeze in Diagnosis of Pulmonary Tuberculosis. J. S. Packard.—p. 1034.
Study of Personality Factors in Group of Neuroses Seen in General Hospital. B. L. Keyes and J. M. Flumerfelt.—p. 1044.
Present Status of Analgesia and Anesthesia from Obstetrician's Viewpoint. T. L. Montgomery.—p. 1048.
Effects of Analgesia and Anesthesia on Prematures. R. M. Tyson. —p. 1051.
Pathologic Lesions of Asphyxia Neonatorum. E. F. Burt.—p. 1053.
*Inadequate and Ill Advised Surgery in Treatment of Carcinoma of Cervix. L. C. Scheffey and G. A. Hahn.—p. 1056.
*Carcinoma of Cervix: Study of 233 Cases Including 103 Five Year Cases with Survival of 33.9 Per Cent. J. R. Johnston.—p. 1062.

**Inadequate Surgery in Carcinoma of Cervix.**—According to Scheffey and Hahn, surgical measures of an ill advised or inadequate nature are being employed too frequently in carcinoma of the uterine cervix. They criticize operative management of this sort and emphasize the contraindications and technical limitations. Radical surgery for carcinoma of the cervix is a recognized method of treatment only on the condition that such a patient has been carefully selected. The lesion must be a relatively early one (groups I and II, Schmitz and League of Nations), the patient should be a reasonably good surgical risk and a radical operation must be performed by an operator thoroughly experienced in its exacting technic. The authors review results observed on 18 patients subjected to operation in whom recurrence was relatively prompt. Two groups consisting of 9 patients each were seen at the Jefferson and Oncologic hospitals of Philadelphia respectively. It is evident from the histories that in each instance either an inadequate operation was performed or proper indications for such an operation were lacking. The short survival of the patients subjected to vaginal hysterectomy is especially appalling when one considers that they were young women with supposedly operable lesions. The surgical procedure was probably not of the type of which Lynch, Bonney and others of similar experience are capable. If the decision to operate is made, it must be a selective operation, not only carried out by one qualified to perform a truly radical operation but based on the premise that the lesion is undoubtedly early, that the patient is an excellent risk and that intracavitary irradiation with radium has been a preliminary procedure. The authors feel that carcinoma of the uterine cervix is best treated with radiation therapy alone. There may be certain patients, carefully selected, who might possibly have a better chance for longer survival when treated surgically by one experienced in the rigorous technic of the radical operation, preceded by irradiation, but in general this is not so. Hence it would be wiser to avoid surgery in the treatment of cervical carcinoma, for a simple type of vaginal hysterectomy or abdominal panhysterectomy is at best only a hazardous and delaying measure in such instances.

**Carcinoma of Cervix.**—According to Johnston cancer of the cervix causes about 15,000 deaths each year in the United States, more deaths than any other gynecologic disease. The author reviews 233 cases of cervical cancer that were registered at the Tumor Clinic of the West Penn Hospital during the last ten years. Twenty-nine per cent occurred in women under 40 years of age. Patients present themselves too late for treat-

ment, as more than 50 per cent had symptoms for six months or longer. The diagnosis of cancer of the cervix is made by careful inspection and palpation of the cervix and by biopsy. At times, when no lesion is visible, a cancer can be detected by palpation, the hypertrophied indurated cervix indicating a carcinoma which can be proved by curetting the cervical canal. Biopsies should be made on all suspected lesions. Up to 1937 most of the cases were treated with radium followed by x-rays. Of late x-rays have been followed by radium. The x-ray dosage varies with the tolerance of the patient, usually from 1,600 to 2,200 roentgens to each of four ports over a period of three weeks. The radium is given in doses of 3,600 to 4,800 mg. hours. Some have had interstitial radiation in the form of four or five 10 mg. needles inserted in the parametrium. Treatment is not repeated unless there is a recurrence as proved by biopsy. The possibility of fistulas and rectal ulcers due to radiation reaction should be remembered and precautions taken to avoid them. The results in 103 five year cases show a survival rate of 33.9 per cent.

## Physiological Reviews, Baltimore

**23**:185-304 (July) 1943

Role of Lipids in Atherosclerosis. E. F. Hirsch and S. Weinhouse.—p. 185.
Nature of Forces Between Antigen and Antibody and of Precipitation Reaction. L. Pauling, D. H. Campbell and D. Pressman.—p. 203.
Physiologic Study of Vertical Stance of Man. F. A. Hellebrandt and Elizabeth Brogdon Franseen.—p. 220.
Noncaloric Functions of Dietary Fats. G. O. Burr and R. H. Barnes.—p. 256.
Quantitative and Qualitative Variations in Normal Leukocytes. C. C. Sturgis and F. H. Bethell.—p. 279.

## Public Health Reports, Washington, D. C.

**58**:969-1000 (June 25) 1943

Studies on Duration of Disabling Sickness: IV. Duration of Disability from Nonrespiratory-Nondigestive Diseases Among Male Employees with Particular Reference to Older Worker. W. M. Gafafer and R. Sitgreaves.—p. 969.
Health Officer's Place in Management of Mental Illness. S. W. Hamilton.—p. 979.
American Q Fever: Experimental Transmission by Argasid Ticks Ornithodoros Moubata and O. Hermsi. G. E. Davis.—p. 984.

## Radiology, Syracuse, N. Y.

**41**:1-106 (July) 1943

Correlation of Disability with Roentgen Findings: Head Injuries. L. H. Osmond.—p. 1.
Correlation of Disability with Roentgen and Clinical Findings in Silicosis: Part I. P. Bovard.—p. 11.
Id.: Part II. J. W. G. Hannon.—p. 13.
Evaluation of Disability in Low Back Injuries. F. L. Schumacher.—p. 18.
Correlation of Disability with Roentgen Findings: The Extremities. E. C. Baker.—p. 23.
Posteromesial Pleural Line. L. H. Garland.—p. 29.
Radiographic Posteromedial Border of Lung or Linear Thoracic Paraspinal Shadow. J. F. Brailsford.—p. 34.
Value of Roentgen Therapy in Carcinomatous Metastases to Bone. E. C. Koenig and G. J. Culver.—p. 38.
Chondro-Osteodystrophy: Morquio's Disease: Case Observed During Pregnancy. P. E. Russo.—p. 42.
Carcinoma of Cervix Complicated by Complete Procidentia: Radiation Therapy. R. A. Harvey and R. N. Ritchie.—p. 48.
Pedunculated Tumors of Stomach Prolapsing Through the Pylorus. T. B. Weinberg and L. Raider.—p. 52.
Effect of Roentgen Irradiation on Hormone Content and Secretion of Adrenal Medulla. W. Raab and A. B. Soule Jr.—p. 56.
Preliminary Notes on Effect of Roentgen Rays on Sulfonamides in Vitro. I. C. C. Tchaperoff.—p. 61.

## Rhode Island Medical Journal, Providence

**26**:79-92 (June) 1943

Sex Hygiene in the Navy. E. C. Smith.—p. 80.
Presentation of Portrait of Charles F. Gormly, M.D., to Rhode Island Medical Society. R. Hammond.—p. 82.
Report of State Chairman for Procurement and Assignment of Physicians to Medical Profession of Rhode Island. H. DeWolf.—p. 86.

**26**:93-106 (July) 1943

Recognition and Management of Rheumatic Fever in Children. A. T. Martin.—p. 93.
Extraperitoneal Cecostomy. A. V. Migliaccio.—p. 96.
Leukopenia in Infections. P. C. Cook.—p. 100.

## Surgery, Gynecology and Obstetrics, Chicago

**77**:1-112 (July) 1943

*Perineal Prostatectomy versus Transurethral Resection for Hypertrophy and Cancer of Prostate. H. H. Young.—p. 1.
Metabolic Studies in Patients with Cancer of Gastrointestinal Tract: XI. Postoperative Hypoproteinemia and Relationship of Serum Protein Fall to Urinary Nitrogen Excretion. I. M. Ariel, J. C. Abels, G. T. Pack and C. P. Rhoads.—p. 16.
Treatment of Gastric Ulcer. E. S. Judd and J. T. Priestley.—p. 21.
Rupture of Uterus: Analysis of 30 Maternal Deaths. C. A. Gordon and A. H. Rosenthal.—p. 26.
Heparin Tolerance: Test of Clotting Mechanism. G. de Takats.—p. 31.
Y Shaped Osteotomy for Correction of Open Bite in Adults. K. H. Thoma.—p. 40.
Osteochondroma of Coronoid Process of Mandible. R. T. Shackelford and W. H. Brown.—p. 51.
Mammary Cancer in Youth. T. de Cholnoky.—p. 55.
Evolution of Circulation in Developing Femoral Head and Neck: Anatomic Study. W. E. Wolcott.—p. 61.
Chemical Considerations Governing Local Chemotherapy of Wound Infections. F. C. Schmelkes.—p. 69.
Maximal Volume of Human Spleen. P. P. T. Wu.—p. 74.
Herniation of Nucleus Pulposus as a Complication of Preexisting Low Back Instability. E. M. Deery.—p. 79.
Posterior Horn Lesions in Meniscal Injury. D. B. Slocum and D. E. Moore.—p. 87.
Ten Years' Experience with Ribbon Gut in Urologic Surgery. O. S. Lowsley.—p. 91.
Pattern of Uterine Motility Throughout Labor with Special Reference to Inertia: Study of 105 Patients with Lorand Tocograph. D. P. Murphy.—p. 101.

**Perineal Prostatectomy versus Transurethral Resection.**—Young analyzed the histories of all patients (now totaling 200) who have come to the Brady Urological Institute complaining of imperfect results following transurethral resection elsewhere. He concludes that in patients with considerably enlarged prostates complete enucleation of the hypertrophied lobes through the perineum gives better results and is no more dangerous than transurethral resection. Prostatitis and painful urination are certainly less common after perineal prostatectomy than after transurethral resection. Another great advantage of the perineal procedure is the opportunity which it affords to make a diagnosis and effect a cure of carcinoma of the prostate. Many conditions, particularly bars, contractures and small hypertrophies, can be dealt with efficiently by transurethral resection, but perineal prostatectomy is distinctly superior for the larger hypertrophies, calculi in the prostate and chronic prostatitis. Prostatism is so complex in its symptoms and so varied in pathologic aspect that it can be handled satisfactorily only by careful selection of the operative procedure best suited to obtain a radical cure. The exclusive use of transurethral resection for all types of prostatic obstruction, even the large and the cancerous, is indefensible.

## Texas State Journal of Medicine, Fort Worth

**39**:53-168 (June) 1943

Scientific Medicine is Fundamental. J. L. Taylor.—p. 59.

**39**:169-220 (July) 1943

Methods of Reducing Mortality and Morbidity in Appendicitis. Q. B. Lee.—p. 175.
Use of Acid Jelly Postoperatively After Vaginal and Cervical Operations and in Nonspecific Infections of Vagina. K. J. Karnaky.—p. 178.
Staphylococcus Infection with Case Reports and Treatment. R. H. Harrison.—p. 185.
Renal Hypertension: Value of Translumbar Arteriography in Its Diagnosis; Preliminary Report. A. K. Doss.—p. 188.
Diagnosis of Intrathoracic Tumors. R. G. McCorkle and C. J. Koerth.—p. 194.
New Era in Medicine. E. W. Bertner.—p. 197.
Diverticulum of Esophagus Duodenum and Colon: Report of Case. M. H. Metz.—p. 200.
Complications and Sequelae of Cataract Operations. E. L. Goar and J. F. Schultz.—p. 201.

## Virginia Medical Monthly, Richmond

**70**:331-382 (July) 1943

Three Gallbladders. W. L. Peple.—p. 331.
Adams-Stokes Syndrome as Complication of Myocardial Infarction: Report of 3 Cases Demonstrating Two Different Underlying Mechanisms. J. R. Beckwith.—p. 336.
Further Observations on Treatment of Eclampsia. M. P. Rucker.—p. 343.
Virus Pneumonia by Contrast with Other Types. J. H. Smith.—p. 353.
Alcohol Abuse, A Public Problem. H. Emerson.—p. 358.
Therapy of Meningitis. J. B. S. Perrow.—p. 363.
Pelvic Appendicitis. L. Smith.—p. 366.
Planigraphy X-Ray Technic. N. Mercer.—p. 369.

## FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

### Annals of Rheumatic Diseases, London

**3**:145-192 (May) 1943

Evaluation of Roentgenologic Findings in Arthritis. J. D. Camp. —p. 145.
Rheumatic Fever and Nutrition. J. F. Rinehart.—p. 154.
*Visceral Lesions Associated with Rheumatoid Arthritis. D. L. Fingerman and F. C. Andrus.—p. 168.
Blood Cultures in Rheumatoid Arthritis (Historical and Personal Observations). T. N. Fraser.—p. 181.

**Visceral Lesions Associated with Rheumatoid Arthritis.**—Fingerman and Andrus examined the records of 192 cases with a diagnosis of arthritis. There were 61 cases of rheumatoid arthritis. The authors apply the term rheumatoid to the severe deforming type of chronic infectious arthritis. The criteria used in selecting these cases of rheumatoid arthritis were as follows: The disease must have been chronic, being present a minimum of several months. It must involve two or more joints. It must have caused deformities of the joints and their adjacent structures. It must be of a nonsuppurative type. The authors examined the clinical records and available pathologic material from 61 patients who had died with chronic rheumatoid arthritis. Lesions indistinguishable from those found in the rheumatic heart were encountered in 19 cases (31 per cent). Six of the patients with rheumatic heart lesions had congestive heart failure as evidenced by chronic passive congestion of the liver. Only 3 persons in the entire group had "Felty's syndrome," or chronic arthritis associated with splenomegaly and leukopenia. There were 6 other patients with splenomegaly along with the arthritis deformans who did not have leukopenia. Amyloidosis involving one or several organs was found in 13 patients (21 per cent). Glomerulitis was found in 8, of which 6 were in early subclinical stages, and the remaining 2 had clinical evidences of glomerulitis.

### British J. Children's Diseases, Dorking, England

**40**:31-62 (April-June) 1943

Teeth of School Children from Point of View of School Doctor. C. Rolleston.—p. 31.
Cause of Death in Newborn Babies. S. Engel and G. H. Newns.—p. 36.

### British Medical Journal, London

**2**:31-62 (July 10) 1943

Circulation in Arterial Hypertension. G. W. Pickering.—p. 31.
*Chemotherapy of Intestinal Infections Treated with Sulfonamide Compounds. A. C. Clay.—p. 35.
Technic of Intravenous Drip Transfusion in Infants. D. MacCarthy. —p. 36.
Trigeminal Neuralgia at an Exceptionally Early Age Cured by Gasserian Alcohol Injection. W. Harris.—p. 39.
Availability of Calcium of Milk. Katharine H. Coward, Elsie W. Kassner and Letitia W. Waller.—p. 39.

**Sulfonamide Compounds in Intestinal Infections.**—Clay reviews 273 cases of bacillary dysentery treated at the City Hospital of Aberdeen during 1941 and 1942, 4 cases of gastroenteritis in infants and 8 cases of paratyphoid B. Of the patients with bacillary dysentery 140 received no drug, 83 were treated with sulfaguanidine, and 50 received sulfanilamide. Adults not receiving chemotherapy were given 2 drachms (8 Gm.) of sodium sulfate night and morning and children 1 drachm (4 Gm.) night and morning. Those receiving sulfaguanidine were given a five day course based on body weight, the initial loading dose during the first twenty-four hours being 0.5 Gm. per kilogram of body weight, followed by a maintenance dose of 0.1 Gm. per kilogram for the next four days. Those receiving sulfanilamide were given a dosage amounting to half the quantity of sulfaguanidine. The tablets were powdered and administered in milk every four hours for the first twenty-four hours and three times daily for about the next four days. Fluids were given intravenously in the form of 5 per cent dextrose in isotonic solution of sodium chloride when necessary, and particular stress was laid on fluid intake by mouth, 8 to 10 pints for adults and proportionately less for children. The stay in the hospital and the number of days during which the stools remained positive were reduced by half for patients receiving sulfaguanidine as compared with those not receiving chemotherapy except in the case of Sonne convalescent carriers, whose stay in the hospital and number of days bacteriologically positive were slightly increased. Of the patients receiving sulfanilamide both the stay in the hospital and the length of time during which stools remained positive were increased, but this may be accounted for by the small dosage of drug and by the small number of patients treated. Neither sulfaguanidine nor sulfanilamide produced toxic symptoms or disagreeable effects. Four patients with gastroenteritis and 8 with paratyphoid B were treated with sulfaguanidine without improvement.

### Deutsche medizinische Wochenschrift, Leipzig

**68**:313-340 (March 27) 1942. **Partial Index**

Surgical Wound Infection and How to Combat It. H. Hellner.—p. 313.
*Problems in Employment of Desoxycorticosterone and Similar Substances in True Adrenocortical Insufficiency. F. Heni.—p. 318.
Tuberculosis of Infants. E. Püschel.—p. 322.
Gastritis, Ulcer, Carcinomas. J. Meinertz.—p. 326.

**Desoxycorticosterone in True Adrenocortical Insufficiency.**—Heni investigated the cause of edema and hypertension in the course of treatment with desoxycorticosterone acetate. He describes observations on healthy subjects and on patients which convinced him that the chief action of desoxycorticosterone acetate is that on the sodium chloride and water economies. Sodium and water are retained in the blood and extracellular spaces and cause increase in blood pressure. If large doses of desoxycorticosterone acetate are used, edema may result. Edema, hypertension and acute shock are not caused by excessive intake of sodium chloride but by desoxycorticosterone acetate. The effect of this substance on the potassium exchange is not as noticeable as that on the sodium. The carbohydrate metabolism is not completely normalized and the fatigability of the patients is not counteracted when signs of excessive dosage appear already in the sodium chloride exchange. Desoxycorticosterone acetate in doses as large as possible was given to 4 patients with Addison's disease. It was impossible to obtain complete restoration in spite of prolonged medication. The patients still felt weak. Complete recovery was obtained only in those whose disease was moderately severe. The authors conclude that although desoxycorticosterone acetate is the best available remedy for Addison's disease their observations indicate that desoxycorticosterone acetate or desoxycorticosterone either are not identical with the adrenocortical hormone or do not represent the only hormone of this organ. Substances chemically related to desoxycorticosterone are capable of exerting favorable effects on the metabolic disturbances of Addison's disease. In severe forms of the disease only progesterone is effective; in mild forms testosterone and low doses of estrone (theelin) effect improvement. These substances do not act by way of the sodium chloride and water exchange, but they improve the glycogen reserve of the organism, particularly that of the musculature. Progesterone might be used in the treatment of severe Addison's disease if moderate doses of desoxycorticosterone cause disturbances in the sodium chloride and water economies.

**68**:341-364 (April 3) 1942. **Partial Index**

Prognosis of Biliary Disorders. F. Munk.—p. 341.
*Study of New Hereditary Agglutinable Factor in Human Erythrocytes. P. Dahr.—p. 345.
Specific Biologic Treatment of Staphylococcic Diseases. H. Gross. —p. 347.
Encephalitis-like Manifestations and Disturbances of Kidney Function in Subacute Lead Poisoning. E. Kirchner.—p. 351.

**New Hereditary Agglutinable Factor in Human Erythrocytes.**—A new hereditary agglutinable factor could be detected in human erythrocytes by guinea pig immune serum produced with blood of rhesus monkeys. In 923 out of 1,129 blood tests, or in 81.5 per cent, the agglutinogen which had been designated as Rh was found, whereas in 206 blood tests, or 18.5 per cent, it was not found. The distribution among the ABO blood groups, the A subgroups and the MNP types seemed to be equal. Studies of 46 pairs of twins suggest that the agglutinogen Rh is hereditary. Results of study in a small number of 17 families are compatible with the assumption that agglutinogen Rh is a simple dominant inherited characteristic.

# Book Notices

**Convulsive Seizures: How to Deal with Them, a Manual for Patients, Their Families and Friends.** By Tracy J. Putnam, M.D., Professor of Neurology and Neurosurgery, College of Physicians and Surgeons, Columbia University, New York. Cloth: Price, $2. Pp. 168, with 12 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1943.

There is a real need for a book to which the victims of convulsions and their families can turn for reliable information. In a large measure this book supplies that need. The task of any book which would instruct patients is a difficult one. Such a book must on the one hand be accurate and sufficiently complete to supply the patient with the required information without at the same time frightening him with rare and unlikely complications of his disorder and without providing just enough information to encourage self medication. A book which would treat of "epilepsy" has one other requirement which it must meet—it must help to brush away the superstitions, fears and inaccurate concepts which have grown up about the convulsive states of unknown origin. If the present book has any one general failing, it is that it is not sufficiently forceful on the latter point. It says but it does not sufficiently stress the facts that in the majority of cases the convulsive seizures can be completely abolished if adequate treatment is begun early and persevered in and that such patients need have no fear of insanity or mental deterioration and can and should lead perfectly normal healthy lives with the same chances to achieve happiness and success in their chosen occupation as other people. The author tends far too much to view "epileptics" as a group, making no effort to separate the mentally retarded with convulsions and those with uncontrollable seizures from the larger and far more favorable group. It is these less fortunate individuals, in particular, that bring down the average of physical fitness noted on page 23.

The author has also been too much impressed with some rather poorly considered statistics on the inheritance of convulsions or a convulsive tendency (pp. 22 and 119). In these statistics, as he noted himself, the rather uncommon instances of definitely hereditary epilepsy were not separated from the far more common sporadic cases. Likewise he has been overly impressed with the value of electroencephalography in selecting individuals with or without the probable potentiality of perhaps producing epileptic children (see p. 151). Not all of those with experience with electroencephalography would agree that the technic has any such capabilities.

Chapter 8, on medical literature, and chapter 9, on the legal aspects of epilepsy, had best be omitted from this book. The latter chapter could well be enlarged for publication in some journal for lawyers or for presentation before legislators. It detracts from the value of this book.

The author is to be complimented for having avoided fads and all peculiar forms of treatment which have found favor in only a few hands. The reviewer's experience would lead him to feel that the restrictions on alcoholic beverages for these patients should be complete and not as lenient as those given here (p. 92).

This book can be recommended to some patients and to more families. No doctor should recommend it without first reading it. It should be placed only in the hands of intelligent and fairly stable people. It is not a book for the overapprehensive, worrisome, easily agitated person. Such people would find more than enough to exercise them here.

**A Handbook for Emergency Commissioned Officers of the Indian Medical Service.** By Lieut. Colonel J. R. Dogra, M.D., I.M.S. Foreword by Major General J. N. Thomson, D.S.O., M.C. Boards. Pp. 202. Bombay: Thacker & Co., Ltd., 1943.

This handbook contains the essential information required to orient completely the emergency commissioned officer of the Indian Medical Service. In addition, the book contains basic reference material which the officer will want to reread until he becomes thoroughly acquainted with it. Any army medical department officer would find this handbook distinctly helpful if he should be destined for service in India or with the Indian army.

It will require four to five hours of careful reading to digest the 136 pages of subject matter. Appendix VII, appendix VIII and appendix IX should be studied carefully first. This procedure will eliminate too frequent reference to the appendix and permit continuous reading. By the use of many abbreviations many facts have been transmitted in comparatively few pages. It is hard to believe that this small handbook can and does include all of the following essentials: organization of the army in India; the medical officer and his relationship to the army; military life; military dress; military courtesy; military discipline; military law; organization, functions and operation of the medical units; duties of medical officers in their various capacities in field and garrison service; field sanitation and preventive medicine; collection and evacuation of casualties; preparation of orders, messages, estimates of the medical situation and medical forms; and, in addition, six appendixes, which include translation of the Geneva Convention, uniform and equipment for emergency commissioned officers, lecture demonstrations, medical standing operative procedures, water sterilization, army forms required by the medical service, medicomilitary definitions and abbreviations.

The medical department officer of the United States Army who reads this book should review our own medical service procedure and installations before he reads it. More enjoyment will be gained thereby in the comparison. For example, he should be able to associate quickly such medical installations as the regimental aid post, advanced dressing station, main dressing station and casualty clearing station with respective stations of our service. He will then be able to trace the casualty through the echelons of evacuation as operated by the Indian Medical Service.

This book reveals a vast amount of experience on the part of the author, who has presented ideal and essential information in a condensed form. It is highly recommended to every Medical Department officer who has interest in medical service of another army or who might serve with the Indian Medical Service.

**The Determination of Blood Groups.** Medical Research Council War Memorandum No. 9. Paper. Price, 10 cents; 4d. Pp. 19. New York: British Information Services; London: His Majesty's Stationery Office, 1943.

The experience gained from the large scale blood group determinations in Britain during the last three years has suggested "that certain procedures, rigidly followed, will reduce errors in grouping to a minimum." To that end the memorandum was compiled by members of the Blood Transfusion Research Committee appointed by the Medical Research Council. Tests for ABO blood groups, subgroups of A, crossmatching tests, preparation and storage of test serums, sources of error and the Rh factor are presented. The completeness of information offered in the sixteen pages of text, the excellent selection of the recommended methods and the emphasis on sources of error combine to make this pamphlet a most valuable contribution to be placed in the hands of clinical pathologists and of technicians who do pretransfusion tests. It can be recommended as the best of its size.

**Essentials of Proctology.** By Harry E. Bacon, B.S., M.D., F.A.C.S., Professor and Head of the Department of Proctology, Temple University Medical School and Hospital, Philadelphia. Introduction by Curtice Rosser, B.A., M.D., F.A.C.S., Professor of Proctology, Baylor University, Dallas. Cloth. Price, $3.50. Pp. 345, with 168 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1943.

The author has taken from his own earlier work portions of those chapters which deal with practical phases of proctology and problems of interest to the physician as he goes about his daily tasks. It is a convenient little volume which should prove valuable to those who do not possess the author's more complete volume. In the foreword Dr. Curtice Rosser wrote "In 'The Essentials of Proctology,' which Dr. Bacon herewith offers to the student, the general practitioner, the surgeon and the specialist in colorectal diseases, is a concise, fluent and detailed exposition of the author's own experience and current practice." This is an accurate appraisal of the character of the book.

# Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

## UNCONSCIOUSNESS AT HIGH ALTITUDE AND OXYGEN SUPPLY

*To the Editor:*—In The Journal, July 24, 1943, there is an article on a parachute jump made by Lieut. Col. William Lovelace from 40,000 feet. The statement was made in the third paragraph that unconsciousness occurred within fifteen seconds without oxygen at 40,000 feet. Since many people can hold their breath for a much longer period of time and even swim under water for longer than fifteen seconds I was wondering whether or not this was a typographic error or whether there were other factors.

Raul Pietri, M.D., Asbury Park, N. J.

ANSWER.—Unconsciousness occurs within fifteen seconds without oxygen at 40,000 feet if the person continues breathing. Once a man is disconnected from his oxygen supply his first expiration empties his lungs and inspiration thereafter takes in air which is so deficient in oxygen that unconsciousness will ensue almost immediately. The actual saturation of blood at 40,000 feet, breathing pure oxygen, is slightly less than normal; consequently the decline in saturation or onset of unconsciousness occurrs with extreme suddenness. This is inherent in the nature of the saturation curve of hemoglobin. If a man at 40,000 feet takes a deep breath and holds it, he will remain in much better condition than if he continues breathing after disconnecting his oxygen supply. It might be further stated that the actual oxygen consumption at 40,000 feet is approximately the same as at ground level or at 300 cc. standard temperature and pressure dry per minute. The actual volume of oxygen in the lungs is approximately 1,000 cc. standard temperature and pressure dry per minute when breathing pure oxygen at 40,000 feet. From this it readily can be seen that the interval of reserve is extremely small even when one is holding the breath.

## APLASTIC ANEMIA AFTER EXPOSURE TO FLOOR WAX AND FLY SPRAY

*To the Editor:*—Can you inform me of the ingredients of Veeco Self-Polishing Wax, manufactured by the American Products Company of Cincinnati and of Wax-Rite Floor Wax, manufactured by the Vestal Chemical Company of St. Louis? A 3 year old child was found to be suffering from a profound anemia and leukopenia. Bone marrow aspiration revealed an aplastic type of marrow. A history of exposure to these waxes was obtained, and it was also learned that the child had been exposed to fly spray used in a dairy barn. Are there any ingredients used in the more common fly sprays which are known to be toxic to the hemopoietic system?

John W. O'Neill, M.D., Eau Claire, Wis.

ANSWER.—The two floor waxes mentioned by name are believed to be of the aqueous soap emulsion type and therefore contain only water as the solvent and none of the organic solvents widely common in some other varieties of floor waxes. Apart from certain hydrocarbon solvents later specified, floor wax ingredients do not cause the clinical manifestations mentioned in the query, although some may induce dermatitis. The organic solvents most likely to appear in floor waxes are toluene, trichloroethylene, naphtha, alcohols and petroleum ether. If benzene or carbon tetrachloride should be utilized potentially, highly dangerous situations might arise. Benzene is known to induce the symptoms described. If any of the floor waxes now questioned has been retained, analyses should be made for benzene although in both instances there is assurance from the manufacturer that no solvent other than water enters the formula. A typical formula for a floor wax of the non-soap emulsion type is East India gum 23 pounds, beeswax 6 pounds, Carnauba wax 20 pounds, Montan wax 8 pounds, naphtha 89 pounds, turpentine 10 pounds, pine oil 3 pounds. Pyrethrum is scarce in this country just now, earlier having chiefly been obtained from Japan. Some insecticides formerly containing pyrethrum as the main insecticidal agent no longer contain it. If, in fact, a pyrethrum spray was used, and this was a well known brand, some petroleum derivative such as naphtha was probably the extracting agent. However, almost any agent might have been employed under present conditions, including dichloroethylene, carbon tetrachloride, trichloroethylene and conceivably benzene. Since exposure probably was limited to a few short periods, this etiologic possibility seems remote.

## HYPERSENSITIVITY TO SULFONAMIDES

*To the Editor:*—Has any work been done to determine how long sensitivity to sulfonamides is maintained and the amount necessary to cause exacerbation? Is it possible to desensitize an individual who is sensitive?

M.D., Massachusetts.

ANSWER.—It is not known from any extensive study how long a patient remains sensitive to sulfonamides. However, isolated cases are on record in which sensitivity was shown to persist for as long as three years. The amount of sulfonamide necessary to cause an exacerbation is usually small, so that a single dose of 0.6 Gm. may cause symptoms in a sensitive person. There are no good methods available for desensitizing patients.

Sensitization to the sulfonamides is usually but not always specific. That is to say, there is usually no cross sensitization. If a patient is sensitive to one sulfonamide compound, another compound can usually be given with safety.

## VITAMIN B COMPLEX AND TINNITUS

*To the Editor:*—What do you feel would be the proper dose of vitamin $B_1$ for a tinnitus, which ear, nose and throat specialists say has no apparent cause other than possible nerve involvement? There is no deafness.

M.D., New York.

ANSWER.—There is no satisfactory evidence that vitamin $B_1$ (thiamine hydrochloride) is of any help in cases of tinnitus or nerve deafness. Since vitamin deficiencies are generally multiple, it would seem wise to give the whole vitamin B complex rather than just the $B_1$ fraction.

An article by Shambaugh and Jennes in the *Archives of Otolaryngology* (**35**:513 [April] 1942) summarizes the literature on vitamin B in deafness and gives the results of use of large doses of $B_1$ in cases of tinnitus in deafness, which were entirely negative.

## BARBITURATES WITH SCOPOLAMINE IN OBSTETRICS

*To the Editor:*—Can you give me information on the use of barbiturates combined with scopolamine for obstetric analgesia? I should like to know the dosage and how soon it could be repeated. Also is it free from the objections that "twilight sleep" has, that is, I suppose it was the morphine part of twilight sleep that was dangerous to the baby rather than scopolamine, wasn't it? Will you please set me straight on this.

George A. Bakke, M.D., Oakland, Calif.

ANSWER.—The barbiturates can be used in conjunction with scopolamine to provide obstetric analgesia. Their effectiveness depends on the drug selected and the amount administered. Unlike morphine, which is primarily an analgesic drug, the barbiturates induce amnesia rather than analgesia. Large amounts are usually necessary to provide desirable effects during labor. The barbiturates, like the opiates, produce narcosis in the newborn. Effective doses will result in asphyxia, which is just as severe as that induced by morphine, or even more severe. An initial dose of such barbiturates as seconal or soluble pentobarbital in combination with scopolamine may be 3 to 6 grains (0.2 to 0.4 Gm.). The barbiturate may have to be repeated in four to six hours to maintain the desired effect. Larger doses have been advocated, but these are not desirable in most instances. Patients in labor under the effect of barbiturates must be constantly attended, for their semicomatose, often delirious, state may lead to unpleasant and serious complications.

## MALARIA IN ALABAMA

*To the Editor:*—The answer to the query of "M.D., Florida" about malaria in southern Alabama, and particularly a "gulf town in Alabama," which appeared on page 1152 of The Journal, Aug. 14, 1943, would not lead an uninformed person to a proper conclusion. The reply errs in stating that "chances of contracting the disease by unacclimated persons would be great." To take a considerable and representative population such as that of Mobile County as a basis of measurement, the vast majority of persons never in their lifetimes have either acute or chronic malaria. If the infection rate is a hundred times as high as the death rate, which for the county varies between 0 and 9 per hundred thousand, the morbidity per year is only between 0 and 0.9 per cent. Those would not be all new cases, of course, but a total including reinfections and infections carried over. The significance of that last point is great because the disease is focalized more than the statement would lead one to believe. Where residence is even moderately dense, Anopheles quadrimaculatus breeding has been mainly controlled, if it ever occurred; or, conversely, where breeding of this mosquito could not be controlled, residence has not become or remained dense. As an example, in the entire Mobile metropolitan or "defense" area last year so few A. quadrimaculatus mosquitoes could be found either in breeding areas or in adult catching stations that there was a repeated threat that all financial aid for survey and control activities would be withdrawn.

It is true that military forces and, in years past but probably not recently, industries have selected sites unfortunately without consideration of conditions which might affect malaria transmission. These, as well as individuals and families, could have settled in the same general areas and perhaps on sites only a mile or two away with a high degree of safety.

O. L. Chason, M.D., Mobile, Ala.
Health Officer, Board of Health.